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# Archives of Dermatology and Syphilology

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## THE "EOSINOPHILIC GRANULOMAS" OF THE SKIN

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PHILADELPHIA

THREE other reports concerning eosinophilic granulomas of the skin appear concurrently with mine in this issue. In them collectively, a full perspective of the world's literature and the history of this disease can be gained, and accordingly these phases of the subject need not be repeated in detail. The same is largely true of the bibliography, the reader is referred to Lever's comprehensive one, which leads into the ten European reports. Incidentally, the reader will be impressed by the abruptness with which the subject has appeared in the American literature and the confusion which exists as to its pathologic significance. Accordingly, this communication can be confined largely to its reports of cases and emphasis on the pathology.

### PRIORITY AND NOMENCLATURE

It is important to determine priority because it is necessary in the attempt to establish a definition for eosinophilic granuloma of the skin. According to the laws of priority in general biology, the original employment of a name takes precedence over all other considerations in nomenclature, without exception. On this basis, the so-called original case of Martinotti, published in 1923, does not qualify, because he did not use specifically the term "eosinophilic granuloma of the skin", Nanta and Gadrat were the first to use the full term, in 1937. For bone, the term "eosinophilic granuloma" was first employed two years later, in 1939, by Finzi. The syphiloïd of cats was described as "*la syphiloïde du chat (granulome éosinophilique)*" by Henry and Bory in 1937. Evidently, then, dermatologists have priority so far as the term "eosinophilic granuloma" is concerned, and the fact that "of the skin" was specified by Nanta and Gadrat in connection with "eosinophilic granuloma" makes it complete. Dermatologists should be careful to use "eosinophilic granuloma of the skin" in full, and surgeons and general pathologists should use "eosinophilic granuloma of bone" in full.

Presidential address delivered at the Sixty-Sixth Annual Meeting of the American Dermatological Association, Hot Springs, Va., June 9, 1946. The paper is modified in view of the fact that other papers on this subject are printed in this issue.

On the basis that Nanta and Gadrat have priority, the characteristics in their case should serve as the type for the disease "eosinophilic granuloma of the skin." Inasmuch as it is a consensus that it is neither an etiologic nor a clinical entity and the histologic features which Nanta and Gadrat postulated are included as type 1 for eosinophilic granuloma of the skin, it remains that the histologic features laid down by Nanta and Gadrat must be accepted as the basis for diagnosis. Inasmuch as monocytes (lymphocytes, plasma cells and histiocytes) are reported in this connection, it would appear that this type of case concerns leukotic disease and belongs in the idiopathic group in the classification which will be indicated later. On this basis, the members of the idiopathic group are the representatives of true eosinophilic granuloma of the skin.

The nomenclature of disease, however, is not so rigid as that in general biology, pathologic processes in tissue are subject to far greater variation "within in the species," as it were, than phases of the structure of plants and animals. It is therefore justifiable to permit a relaxation of the requirements implied by Nanta and Gadrat's original description of the histologic structure and to expand the scope of their findings (and/or modify them) when it appears to be justified. In short, as matters have turned out, these authors inaugurated simply an inquiry into the significance of excessive eosinophilia in cutaneous lesions. The earlier reports of the disease indicate that the authors arrived rather promptly at the conclusion that it was not a clinical or etiologic entity. It revolved in the atmosphere of such diverse leukotic diseases as Hodgkin's disease and mycosis fungoides.

To summarize, dermatology has priority in the use of "eosinophilic granuloma" and Nanta and Gadrat of "eosinophilic granuloma of the skin." The term was used originally by reason of the (eosinophilic) histologic reaction. At present writing, too, it connotes only the processes of eosinophilia. Therefore, the term can be used with the utmost latitude in any dermatosis with great eosinophilia in the tissues. One must not fall into the error that it signifies a specific causation that covers all cases of this pathosis.

As to priority in the literature of this country, credit belongs to Lewis. He was the first to present a case under the particular title of "eosinophilic granuloma"; this was presented at a meeting of the New York Academy of Medicine, Section of Dermatology and Syphilis, on May 3, 1943<sup>1</sup>. My patient was presented on Nov 17, 1944 before the Philadelphia Dermatological Society<sup>2</sup>.

1 Lewis, G. M. A Case for Diagnosis (Eosinophilic Granuloma?), *Arch Dermat & Syph* **49** 375 (May) 1944.

2 Klauder, J. V., and Weidman, F. D. A Case for Diagnosis (Eosinophilic Granuloma?), *Arch Dermat & Syph* **53** 558 (May) 1946.

## MATERIALS

Dr Joseph V Klauder first stimulated my interest in this subject when he generously placed his patient at my disposal and supplied the clinical photograph and two lots of material from biopsy specimens. This forms the basis of what I shall refer to as "our case." Too, prior to the publication of their papers in this issue, Drs Lewis and Cormia and also Dr Lever furnished me with histologic sections and with copies of their manuscripts. Dr Buley<sup>3</sup> did likewise. The contribution of Dobes and Weidman in this issue speaks for itself. The names of no less than four other physicians will appear later from whom I have received tissues and data which bear on the subject. All these gentlemen have



Fig 1 (our case) —Lesion of five months' duration (in November 1944, i e, at the tenth month of the disease)

permitted me to use their materials without reservation and deserve credit as co-authors in this paper, it would be restricted indeed but for their generosity. Altogether, I have been able to study sections from 9 cases.

## REPORT OF OUR CASE

The following report extends largely through the first year of the disease. At present it is of two years' duration (as of October 1946), but during the last ten months the patient has passed into other hands.

In P. R. H., a white man aged 50 years, there developed a lesion over the right scapula about January 1944. It was treated during March and April

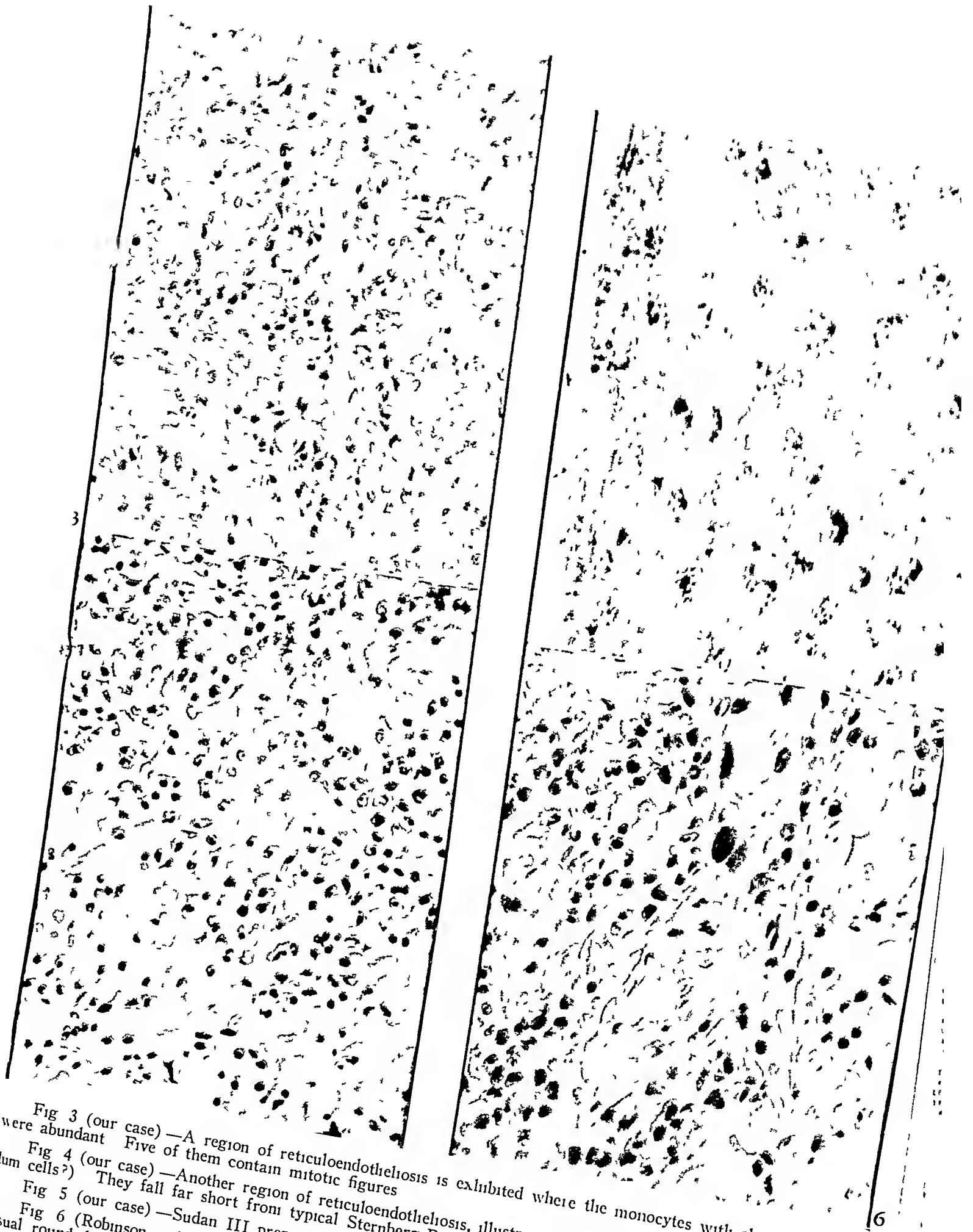
3 Buley, H. M. Eosinophilic Granuloma of the Skin, *J. Invest. Dermat.*, to be published.

with roentgen rays (1,200 roentgens, divided in six doses, with no filter) by a roentgenologist, and it disappeared. It was reported as being firm, elevated and ovoid, measured 4 by 2 cm and was centrally ulcerated. Four months later a lesion appeared on the left leg. The roentgenologist administered five doses



Fig 2 (our case) —The pseudoepitheliomatous hyperplasia. The cellular infiltration was relatively scanty in the upper parts of the skin, as seen here. Deeper, it was densely compacted.

of 1,000 roentgens each, filtered through 0.1 cm of aluminum. The lesion improved considerably. In June an ulcerated lesion appeared in the left ear. It received 500 roentgens, divided into five doses, unfiltered.



- Fig 3 (our case) —A region of reticuloendotheliosis is exhibited where the monocytes with clear cytoplasm were abundant. Five of them contain mitotic figures.
- Fig 4 (our case) —Another region of reticuloendotheliosis, illustrating the supposedly monocytic cells (reticulum cells?). They fall far short from typical Sternberg-Reed cells.
- Fig 5 (our case) —Sudan III preparation demonstrating fat in the epidermis.
- Fig 6 (Robinson and Ketron's case) —The hyperplastic endothelial cells of the blood vessels are not of the usual rounded form that appears in inflammatory reactions.



I first saw the patient about ten months after the onset of the disease. The concha of the ear was filled by a mass (five months' duration), which concealed the external auditory canal. Its center was ulcerated, bled easily and was covered with a yellowish membrane. Part of the tumor extended onto the anthelix in the form of a plaque with a smooth intact surface, and another portion extended onto the crus helix. The plaques were firm, elevated up to 2 to 4 cm above the *niveau* and evidently infiltrated. Under wet antiseptic dressings, the ulcer healed partially and the bleeding became less pronounced. During the subsequent two weeks the mass became larger, and pain developed in the ear, which radiated to the throat and down the neck.

The patient had never traveled beyond the United States, he had not been away from the vicinity of Philadelphia for a number of years. There was no history of syphilis. In November and December, 1,300 roentgens were administered to the ear in twelve doses, and in January 1945 1,000 roentgens was given in ten doses, all of these at 200 kilovolts and with 0.5 mm copper filtration.

Roentgenograms of the skull demonstrated that the bone underlying the lesion was not involved in the processes, and several roentgenologic examinations of the chest, skull, bones, pelvis, extremities and spine failed to reveal additional lesions. About January 1946, the entire lesion was excised, involving amputation of the ear. Skin grafts did not take. The general physical state of the patient has been steadily downhill since that time, and a fatal termination is expected. A roentgenogram made in April 1946 demonstrated that the lesion had infiltrated into the pterygomaxillary fossa around the roots of the fifth, sixth, seventh, ninth, tenth, eleventh and twelfth cranial nerves. Roentgen treatment (up to 2,700 roentgens) was highly effective at first, but the disease advanced again in August 1946. Up to October 1946, none of the superficial lymph nodes had become enlarged and disease in other parts of the body could not be demonstrated.

The laboratory investigations were not particularly significant. The Wassermann reaction of the blood for syphilis was negative. The red blood cell count was normal, and the hemoglobin content measured 74 per cent. Of the 6,250 leukocytes, only 4 per cent were eosinophils, the other forms were within normal range. The Schilling index showed metamyelocytes 0, stab cells 11 per cent and segmented forms 59 per cent. The multiple index was 30, a relatively normal shift. The lesions were not influenced by three intramuscular injections of bismuth subsalicylate and the oral administration of potassium iodide in doses ranging up to 30 grains (2 Gm) three times daily.

*Histologic Examination*—A biopsy specimen was secured on Nov 10, 1944. The epidermis was ulcerated and acanthotic, highly edematous and sparingly infiltrated with degenerated (apparently neutrophilic) polymorphonuclear leukocytes. The interpapillary pegs were bizarre and extended as long snags to the midcorium. This was an expression of pseudoepitheliomatous hyperplasia, such as occurs frequently in connection with the regeneration of the epidermis in connection with ulceration. The mimicry of cancer was close indeed.

The corium was occupied solidly by inflammatory cellular infiltration, barring an edematous zone which lay immediately below the epidermis. The infiltration was so dense that but little of the normal collagenous tissue could be identified. It was disposed on a reticuloendothelial framework, which was dense in some places but so loose in others as to suggest lattice fibers. Everywhere, blood vessels were extremely numerous, thin walled and sometimes associated with small hemorrhages.

The cells concerned varied from place to place. Lymphocytes and eosinophilic polymorphonuclear leukocytes appeared everywhere, and the latter were so

sharply focalized at some places as to constitute miliary abscesses. An additional type of cell approached the Sternberg-Reed cell closely. It was scatteringly distributed and never in groups. The cytoplasm was rarefied and indeed invisible in some cases. The cell membrane could not be recognized. The nucleus was large and rounded, and a few examples were indented. Many were in mitosis, but, on the whole, they were poor in chromatin. In short, they were probably monocytes which were in a state of hydropic degeneration.

Micro-organisms could not be identified within the abscesses or elsewhere.

A second biopsy was performed on Nov 15, 1944. Barring certain quantitative differences, the reaction was the same as that in the first biopsy specimen. Thus the degree of eosinophilia was definitely less, although it was still great in one or two localized regions. Mitotic figures were fewer, but the monocytes were much more numerous.

#### PATIENTS NOT SEEN CLINICALLY BY ME

The patients in the following cases came to my attention as part of the routine histologic work of the laboratory during the two and one-half years which have elapsed since our patient aroused the subject of eosinophilic granuloma of the skin.

CASE 1—H J (a patient of Drs Harry M Robinson and Lloyd W Ketron), a Negro man, was first seen and examined at the University Hospital of the University of Maryland School of Medicine and College of Physicians and Surgeons on July 16, 1945. The duration of his disease was said to have been one month. On the glans penis there were numerous discrete and grouped, round, shiny nodules 2 to 3 mm in diameter. They were concentrated around the urethral orifice and the corona. A slight, dark red discharge escaped from the urethra. The cystoscope passed easily, the prostatic urethra was found to be congested and the verumontanum engorged and bleeding. It was the urologist's impression that verumontanitis was present. The serologic test of the blood for syphilis elicited a negative reaction. Both the Frei and the Ito-Reenstierna test gave positive reactions. The white blood cells numbered 10,150 and the red blood cells 4,970,000. The polymorphonuclear neutrophils constituted 27 per cent, the lymphocytes 55 per cent and the eosinophils 18 per cent. The hemoglobin content measured 16.1 Gm. The sedimentation rate was 40 mm corrected to 34. The hematocrit reading was 46 per cent.

*Microscopic Examination*—A biopsy was performed on Nov 19, 1945. Two types of pathologic change were represented in the tiny nodule. The first process was an extensive hyperplasia of highly dilated capillaries, which was so extreme as to suggest endothelioma. However, the blood vessels were distributed regularly and uniformly throughout the lesion and were uniformly spaced and normally formed. Moreover, the lining endothelial cells, although hugely enlarged, were disposed at regular intervals in a single layer over the linings of the capillaries. They were striking by reason of their huge size, broad cytoplasm and polygonal outlines. They were not crowded or at all anaplastic, such as should be the case for endothelioma. In short, the huge enlargement of the individual cells was accompanied with comparatively little numerical increase.

The second process consisted in an extreme, diffuse infiltration of eosinophilic polymorphonuclear neutrophils. There was not any noteworthy connective tissue or other kind of stroma.

*Summary and Interpretation*—A localized nodular eruption on the glans penis of one month's duration, which may or may not have had a relationship to associated disease of the prostatic region, had a certain resemblance clinically to molluscum contagiosum. The reactions of the tissue were most puzzling, but hemangioendothelioma appears to be excluded. The uniformity and indi-

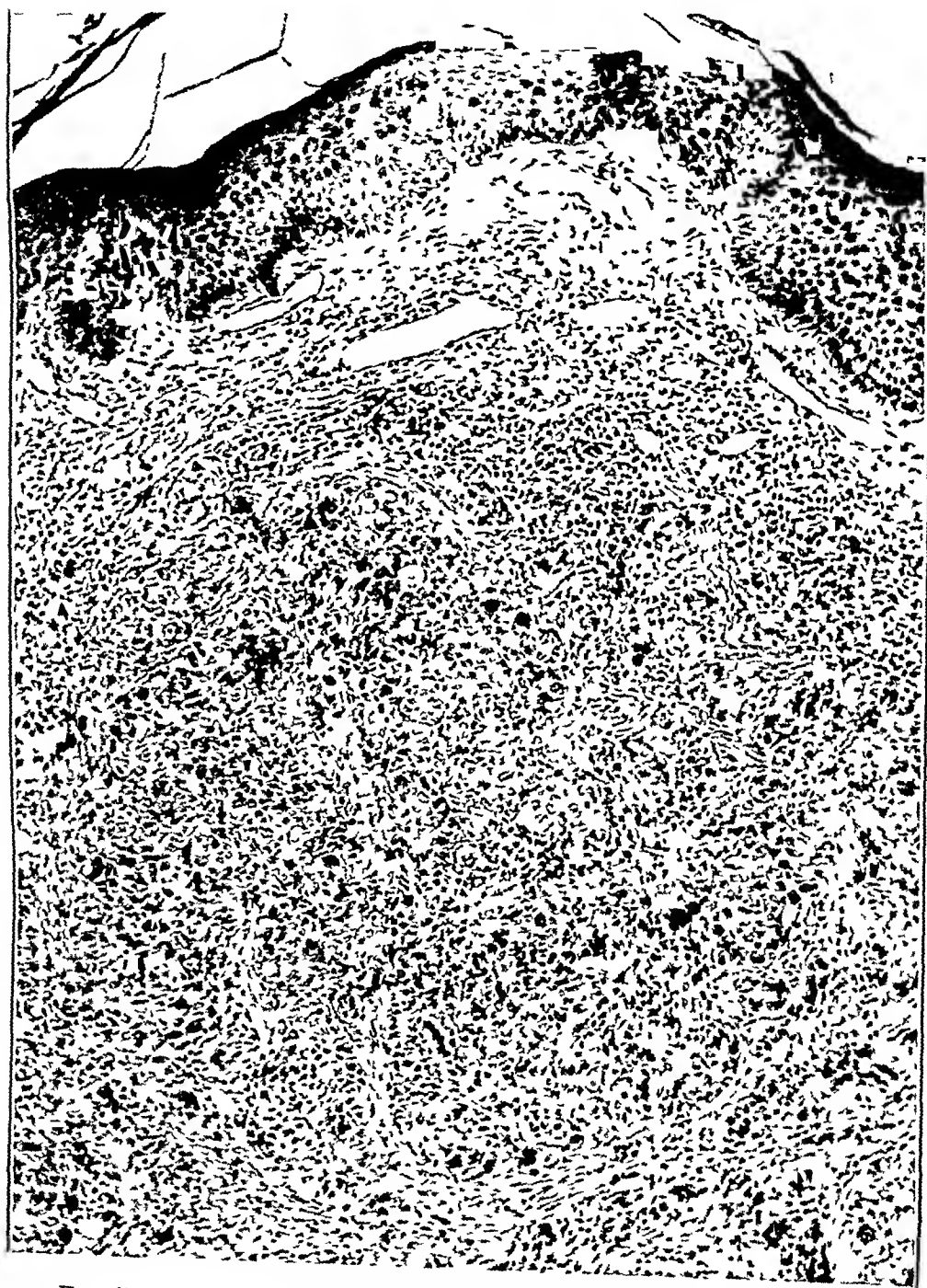


Fig 7 (Robinson and Ketron's case)—The angiomatoid patterning

viduality with which the endothelial cells are reacting appears to exclude an inflammatory causation for the hyperplasia and points more reasonably toward some leukotic factor. The extreme eosinophilia is the only feature which suggests any relationship to eosinophilic granuloma of the skin.

CASE 2—A white woman (a patient of Drs Earl Runyon Tyler and John D Miale), aged 26 and in excellent health, observed first a nodule over the left eyebrow in August 1945. It enlarged slowly, became purplish red and was slightly itchy. Subsequently, lesions appeared scatteringly over the body but with a predilection for the arms and face. They were still slightly itchy, attained a diameter of about 2 cm and eventually disappeared, leaving only a slight induration. There was not any lymphadenopathy, and the cells in the peripheral circulating blood were normal in all respects. During three months of treatment with arsenic, the lesions disappeared, leaving a solitary lesion on the forearm. The clinical features were only suggestive of mycosis fungoides.

Microscopically, the epidermis was decidedly acanthotic and exhibited in general the (edematous) features of mycosis fungoides but without any Pautrier's abscesses. The processes in the corium were not those of mycosis fungoides. There was not any reticuloendothelial network, and the infiltrating cells were not disposed in the widespread way that is usually the case for mycosis fungoides.



Fig 8 (Robinson and Ketron's case) —Lesions on glans penis

but were confined within mantles around the blood vessels and appendages. At two places, though, they infiltrated the subcutaneous fat. Although lymphocytes appeared in a few localized regions, eosinophilic polymorphonuclear neutrophils dominated the scene, they were massed in the places where the infiltration was the more extensive, particularly toward the subcutaneous fat. A few hyperplastic endothelial cells and certain other large cells, which were presumably monocytes, were intermingled. It was not possible to identify any indented or reniform nuclei such as would prove the presence of monocytes.

*Summary and Interpretation*—In the absence of generalized lymphadenopathy or of an adequate histologic picture, it is hazardous to pronounce a final diagnosis of mycosis fungoides to say the least, and the absence of severe itching adds to the uncertainty. The disease was probably of the order of a low grade cellulitis. This case is included in my series as a matter of record in connection with eosinophilic granuloma of the skin and because mycosis fungoides was seriously considered by Lapiere in his case. In any event, the eosinophilia was impressive to say the least.

CASE 3—C C (a patient of Dr Louis Goldstein), a white woman aged 38 and single, had suffered from deep-seated papules on the upper and lower extremities for seven years. They underwent superficial ulceration and disappeared, leaving pigmented macules.

A biopsy was performed on April 21, 1945. Microscopically, a localized area of reticulosis was observed in relation to a hair follicle. Young blood vessels ramified richly through it. Most of the cells in the case were lymphocytes, but polymorphonuclear eosinophils predominated in certain regions. Typical Sternberg-Reed cells were sparingly intermixed. The eosinophils did not appear in the tissue surrounding the granuloma, here only a heavy mantle of lymphocytes appeared around the blood vessels.

A second biopsy was performed May 26, 1945 on the back of the right leg. By this time a solitary lymph node in the axilla had become enlarged, and up to October 1946 it remains the only one. The reaction differed from that in the first biopsy specimen in that the regions of polymorphonuclear infiltration were more numerous and that the histiocytes were seldom of the typical Sternberg-Reed type. The appearances were not nearly so convincing for Hodgkin's disease as those in the first specimen. Indeed, considered purely from the histologic viewpoint, they were not even suggestive.

Further biopsies were performed on May 4, 1946 on material from lesions on the inside of the right thigh and the front of the left forearm. At this time the lesions were prurigo-like. Singularly, in neither of the lesions was there enough eosinophilia to attract attention. A remarkably heavy mantle of reticulo-endothelial tissue comprised broad tracts around certain blood vessels in the midcorium. The cells were largely lymphocytes, but reticulum cells were also abundant. Monocytes could not be identified. Only a few small clusters of polymorphonuclear neutrophils were widely scattered here and there. In sections stained by Giemsa's method, a few mast cells were brought to light but gave no additional information. Neither in the lesion from the forearm nor in the lesion from the leg were there any of the features of Hodgkin's disease or eosinophilic granuloma. In short, at this stage of the disease the leukotic processes of Hodgkin's disease appeared to be quiescent, at least in the skin. Apparently such processes occur in waves, and accordingly the histologic picture varies from time to time.

*Summary and Interpretation*—This case should be regarded as one of Hodgkin's disease in which the cutaneous lesions clinically were of the non-specific type, i. e., prurigo-like. The histologic picture of Hodgkin's disease was exhibited satisfactorily only in the first biopsy specimen, the development of lymphadenopathy was necessary to establish the diagnosis.

CASE 4—Mrs von T (a patient of Dr Carroll S Wright) presented an ulcerated lesion on the vulva, which had been present for one year. It had a slightly elevated border. The Wassermann reaction of the blood was negative on several occasions, and cultures had been made which were without significance. Examinations of the peripheral circulating blood resulted in normal findings. Dr Wright removed the lesion by cauterization on March 28, 1945, this was followed by healing. Two lesions developed subsequently which were also cured by cauterization.

Microscopically, a quasituberculoid reaction was observed in the base of the ulcer. It constituted a superficial zone, underlain by a remarkable infiltration by eosinophilic polymorphonuclear leukocytes (no eosinophilic myelocytes). Scarcely a neutrophilic leukocyte could be discovered anywhere in the section.

The tuberculoid tissue consisted of solidly packed "epithelioid cells," but in no case were they localized into miliary granulomas and there were not any giant cells. Some of the epithelioid cells were indented or reniform, and a few were in mitosis. The endothelia of the blood vessels were swollen, but, in spite of the fact that a few mitoses were occurring in them, they were not notably hyperplastic. A few foci of necrosis were not surrounded by the special zones of cells, such as is characteristic for tuberculosis.

A third lesion was excised on Sept 15, 1946. Fixed in solution of formaldehyde it was definitely yellow, but it was not adequate for frozen sections and staining for lipids. The order of reaction was that of the first lesion, with certain quantitative differences. Lymphocytes were confined to positions adjacent to blood vessels. Now the monocytes were so closely packed that a reticulo-endothelial framework could scarcely be recognized. The nuclei of some were huge, others were indented or reniform and some were in mitosis. Contrary to the first lesion, neutrophilic leukocytes were in a large majority. Eosinophils, some of which were mononuclear and others polymorphonuclear, occurred only in nests here and there throughout the lesion, i e, they were not nearly so numerous as in the first biopsy specimen. The lumens of blood vessels, although crowded with eosinophils, did not contain any monocytes. The reaction was not at all tuberculous, it stimulated aleukemic reticulosis, but with eosinophils. This was evidently an older lesion, because the infiltration extended much more deeply and the polymorphonuclear cells were far fewer.

*Summary and Interpretation*—A histologically tuberculoid lesion of the vulva, accompanied with extreme eosinophilia of the tissues, may or may not have been the expression of most atypical, diffuse tuberculosis in which the monocytes assumed a form other than that of the typical epithelioid cell. However, the indented and reniform nuclei are foreign to tuberculosis as it is conventionally conceived. This case is included in my series largely because the monocytes in the case took a quasiepithelioid form similar to the ones which have been described by Dobes and Weidman in this issue in one of the lesions of their patient with Hodgkin's disease. In eosinophilic granuloma of bone, too, the monocytes can assume this form.

#### ANALYSIS AND CLASSIFICATION

The cases which have been published in the literature have already been abstracted and discussed in the papers by Lever and by Lewis and Cormia in this issue. There is general agreement that the clinical picture is so variable that it cannot serve of itself either as a basis for diagnosis or as the establishment of an entity. In every case, it was the eosinophilia which originated the diagnosis. The same must be said of the 5 patients whose case histories are recorded herein.

The details of the histologic features, too, have been sufficiently covered by Lever and by Lewis and Cormia. The histology is far more constructive toward the establishment of an entity than through clinical channels. It will be noted that there are but two features common to all the cases, namely the deep location of the lesions and the eosinophilia. Thereafter, histiocytes received mention frequently, incidentally, it is probable that some of them were numbered among the "eosinophils" simply by reason of the eosinophilic granules that they phagocytosed.

after such granules had escaped from other kinds of cells. Polymorphonuclear neutrophils were described less frequently (Dobes and Weidman and Martinotti's third case). Monocytes received frequent mention, but, inasmuch as this type of cell can be interpreted on such a variable basis at the hands of different authors, the significance of all the monocytes cited is indefinite indeed. Still, there can be no question that they were frequently concerned. Eosinophilic myelocytes were included by Pasini and plasma cells by Freund. The "monstrous cells" described by Lapiere could have been of the same order (monocytes) as those described by Dobes and Weidman, and, inasmuch as Lapiere found a picture in the lymph node which resembled that in Hodgkin's disease, it is possible that both of the cases were in fact ones of Hodgkin's disease. I found epitheloid cells in Wright's patient and in one of the lesions in the case of Dobes and Weidman.

In short, the types of cells are indeed diversified, but the pleomorphism is of a different order from that of mycosis fungoides. This is not surprising in cases in which cells of the reticuloendothelial system are concerned, there are similar variations within one and the same entity, such as illustrated by Hodgkin's disease. Accordingly, a definite formula for cells must not be insisted on for the diagnosis of eosinophilic granuloma of the skin.

*Suppuration* Suppuration was conspicuous by its absence in both the clinical reports and the histologic sections. It is not surprising when one considers the small numbers of neutrophilic polymorphonuclear cells that appear in the sections, although the eosinophilic ones can occur in such large and solid masses that they qualify as eosinophilic abscesses. The latter term must be modified at once though, because liquefaction is not in evidence, they would have to be "dry abscesses."

An explanation of such dryness is at hand because eosinophilic polymorphonuclear cells do not produce the proteolytic (liquefactive) enzymes in human beings in the way that the neutrophil ones do. It is worth while to compare this situation with that in birds. In these, clinical suppuration is practically unknown, even in diseases that are known to be of the most acute infectious nature and in which suppuration would be expected if it were mammals that were affected. Suppuration is replaced by caseous material. Veterinarians advance the similar explanation for this dryness, namely, an absence of proteolytic enzymes in the eosinophilic leukocytes which dominate the picture, but they extend the idea to include the neutrophilic ones.

Thereafter, features other than the cytologic are available and must be drawn on for purposes of evaluation of the processes, such as the patterning of the pathologic tissues, vascular relationships and reticuloendotheliosis, these, especially the latter, are of surpassing value. With their help, I have ventured to arrange a histologic classification such as

is indicated in the table. The classification is based on the fact that some of the conditions, at least, exhibit reticuloendotheliosis and might be leukotic in nature, in the sense of Hodgkin's disease. In a second category, certain cases are included in which there is not any reticuloendotheliosis, the eosinophilic leukocytes are simply exudative (or histiogenetic?) and not associated with monocytes or other cells which might signify a leukotic factor in the case. In some of the cases, the evidence is clearcut, for example, unequivocally reticuloendothelial conditions are illustrated in those of Pautrier and of Dobes and Weidman and the "symptomatic" ones in the case of Lewis and Cormia. They

*Classification of Eosinophilic Granulomas of the Skin*

A Idiopathic (leukotic)

- |  |                              |
|--|------------------------------|
| 1 Eosinophilic myelopoiesis only, theoretic, and cases may never be established, an aleukemic myelogenous leukemia that is dominantly eosinophilic |                              |
| 2 Endotheliosis with eosinophilia  | (Robinson and Ketron's case) |
| 3 Reticuloendotheliosis with eosinophilia  | (Dobes and Weidman's case)   |
| Hodgkin's disease (with lipoidosis)  | (Goldstein's case)           |
| Mycosis fungoides or Hodgkin's disease   | (Lapierre's case)            |
| Mycosis fungoides (atypical)   | (Freund's case)              |
| Lymphosarcoma  | (Cerruti's case)             |
| Aleukemic reticuloendotheliosis  | (Pasin's case)               |
| Aleukemic reticuloendotheliosis with lipoidosis  | (Our case)                   |

B Symptomatic (inflammatory, including specific granulomatous infections)

- |  |                           |
|--|---------------------------|
| 1 Erythema multiforme perstans (Loeffler's syndrome) | (Lyon and Kleinhaus)*     |
| 2 Ids, with eosinophilic periarteritis               | (Lewis and Cormia's case) |
| 3 Erythema elevatum diutinum                         | (Lever's case)            |
|  | (Buley's case)            |
|  | (Wigley's case)           |
| 4 Orificial tuberculosis                             | (Wright's case)           |
|  | (Nanta and Gadrat's case) |
| 5 Specific infections (syphiloid of cats)            | (Bory)                    |
| 6 Nonspecific ulcer of the leg                       | (Martinotti's case 1)     |
| 7 Yeast infection                                    | (Martinotti's case 2)     |
| 8 Bullous erythema multiforme ?                      | (Martinotti's case 3)     |
| 9 Cellulitis ?                                       | (Tyler and Miale's case)  |
| 10 Not diagnosable                                   | (Pautrier's case)         |

\* Not known that the cutaneous lesions were eosinophilic. This remains to be shown.

may serve as type cases. Inadequacy of histologic descriptions prevents a satisfactory, clearcut assignment of some of the cases reported.

I am encouraged to employ this basis for classification because two of the so-called lymphoblastomas, namely, mycosis fungoides and Hodgkin's disease, have been implicated already by Pautrier and by Lapierre. Moreover, Lewis and Cormia have taken a forward step by segregating their case as one of eosinophilic periarteritis, it would fall into my "symptomatic" group. In any event, my classification may serve as a point of departure for the further appraisal of eosinophilic granuloma of the skin. The limitations imposed by the difficulty of histologic interpretation within the field of the leukoses speak for an uncertain basis for appraisals in any circumstances, and accordingly the

classification submitted cannot be perfect in expressing a true biologic situation. It is to be emphasized that the classification is only a working plan.

After having postulated the idiopathic and the symptomatic groups of cases, I have taken a step farther. Thus, by combining the clinical and the histologic features, I have attempted to identify some already established dermatologic entity in the case but to which eosinophilic features have been added. In the idiopathic group the case of Dobes and Weidman serves as an example in which it was Hodgkin's disease to which the eosinophilia was added, and for the symptomatic group Lever's case of erythema elevatum diutinum may be taken as the type. The line of reasoning would parallel here the one which I have followed in studies of xanthoma. To cite but one example, it is thoroughly established that the histologic picture of xanthoma may develop within scar tissues<sup>4</sup> to the extent, indeed, that the original scar tissue in the sections is not recognizable. That is, only the clinical history of a preexisting scar established the case. In other words, it is conceivable that in eosinophilic granuloma of the skin, too, an intercurrent eosinophilous disease or at least pathologic substrate can modify or obscure an otherwise readily diagnosable entity.

The message to be derived from this theory is that in future studies of eosinophilic granuloma of the skin this possibility should be reckoned with. I do this in spite of Buley's opinion that it would add confusion. I would submit that, as I have plotted out the 19 cases in my classification, an illustration is supplied as to the diversity, at least, of conceivable dermatologic pathoses within which the syndrome of eosinophilic granuloma might occur, in this light, the dermatologist should not be hesitant in maintaining his clinical diagnosis of some well known entity simply because the eosinophilic syndrome appears in the sections. Indeed, it is predictable that additional dermatoses will be placed on the list. Moreover, it was in this light that an over-all view of the cases permitted the two major subdivisions in the classification, and, after the two different pathologic bases which are concerned (leukotic and inflammatory) are revealed, it becomes obvious that the prognosis is radically different in the two.

Buley's discussion of Sulzberger concerning histamine is welcome here in helping to explain some of the discrepancies that arise in eosinophilic granuloma of the skin, "such substances capable of producing a dense eosinophilic infiltrate as those described might well alter the clinical manifestations of a well known entity to such a far reaching

4 Weidman, F. D., and Boston, L. N. Generalized Xanthoma Tuberosum with Xanthomatous Changes in Fresh Scars of an Intercurrent Zoster, *Arch. Int. Med.* 59:793 (May) 1937.

extent that the typical character of a certain disease would be partly or entirely lost" The point is that in the presence of such disturbing factors well known entities would become more readily admissible as such (in spite of their diagnostic shortcomings) when complicated by the eosinophilic syndrome

The application of the foregoing facts in the diagnosis from histologic sections is clear Thus, when the eosinophilia is so great as to arouse thoughts of eosinophilic granuloma of the skin, the attempt should be made to determine whether the associated reaction is the reticuloendothelial one or the perivascular one The former will at once connote the considerations recorded for the idiopathic group and the perivascular ones those of the symptomatic In the case of reticuloendothelial reactions, the attempt should be made to determine whether it is inflammatory or leukotic, this is usually a difficult task, and there should not be any hesitation in consulting the expert hematologist

#### SIGNIFICANCE AND ROLE OF THE EOSINOPHILIA

For the purposes of this communication the contributions of Lever and especially of Lewis and Cormia in this issue supply adequate outlines of the circumstances in which eosinophilia in general may occur The literature is gigantic, but a perspective of the whole situation has been supplied by Ringoen<sup>5</sup> It is clear that an eosinophilia of the blood can arise in many different ways, but unfortunately the literature is not nearly so satisfactory in respect to eosinophilia in the fixed tissues However, it has long been an accepted fact that eosinophilia both of the blood and of the fixed tissues has been conspicuous where cutaneous disease was concerned The significance of this is not known, but the importance of the skin in allergic processes and the eosinophilia which is so conspicuous in allergy must have a bearing in the situation In any event, there are agencies extant for inducing eosinophilia in both the idiopathic (reticuloendothelial) and the symptomatic (inflammatory) groups indicated in my classification It is not necessary to elaborate in the case of the former group because it already implies a lesion of hemopoietic tissue where myelopoiesis (including eosinophilia) can be taken for granted

In the case of the symptomatic group though, it is recommended that in the future the studies of Buley be followed as a pattern in an attempt to discover an underlying cause for the eosinophilia Too, in view of the frequency with which authors have quoted both mononuclear and polymorphonuclear eosinophils in the skin, the attempt should be made to establish the identity of the ones which were designated as

<sup>5</sup> Ringoen, A R Eosinophile Leucocytes and Eosinophilia, in Downey, H Handbook of Hematology, New York, Paul B Hoeber, Inc, 1938, vol 1, p 181

"mononuclear." Are they monocytes or what? Inasmuch as the details of these cells are inadequate in histologic sections, it is recommended that impression preparations of tissues be made, such as have been urged by Winer<sup>6</sup> in the study of Hodgkin's disease. This is highly important to dermatologists, by such a procedure much might be learned in respect



Fig 9 (Buley's case) —The type of reaction in the symptomatic group, i e., no reticuloendotheliosis but a vasculitis and perivasculitis

to an unsuspected leukotic role. The studies should be conducted along the same lines that a hematologist follows for essential disease of hemopoietic tissue.

<sup>6</sup> Sweitzer, S. E., and Winer, L. H. Ulcerative Hodgkin's Disease and Lymph Node Imprints, *Arch Dermat & Syph* 51:229 (April) 1945

In consideration of eosinophilic granuloma of the skin in all its aspects, although it is neither an etiologic nor a clinical entity, it is proper to set it up as a histologic entity or syndrome in the setting of eosinophilia. Thus, it satisfies the definition of an entity because the eosinophilia is so extreme and because even at this early date in its history it has been found to revolve around leukotic conditions like Hodgkin's disease and mycosis fungoides, on the one hand, and around arteritis (Lever, and Lewis and Cormia), on the other. In all probability, other categories of dermatologic disease will be added. It is an entity within the histologic field in the same sense that erythema nodosum and erythema multiforme are entities within the clinical field. For example, in erythema multiforme the etiologic factor is not a single one, there is much variation in the distribution of lesions in the case and even in the appearance of the lesion, and yet the ensemble contains sufficient characteristics to identify it as an entity.

In short, the concept of eosinophilic granuloma of the skin as an entity is a useful one if nothing else. Its occurrence points along certain definite avenues which should be followed toward the discovery of an etiologic factor. On the other hand, its limitations must be definitely understood. It is only a tissue eosinophilia, but it still has disease associates that are significant. It is not etiologically diagnostic. It does not connote any special order of tissue process that is peculiar to any clinical entity of the skin, such as is the case for eosinophilic granuloma of bone, unless investigations of the future prove otherwise. I have employed "eosinophilic granulomas of the skin" (i e, in the plural) in the title of this paper because most physicians will desire a term that will cover the pathosis in all its aspects. etiologic, clinical and histologic, this communication is an example of a situation in which "granulomas" is indicated. When discussing an individual case, it is "one of the eosinophilic granulomas of the skin."

Both in the literature and in some of my personally studied cases, the eosinophilia has not been constant, either in blood or in tissue. This appears to speak for waves of the eosinophilogenic influences. Naturally this introduces its problems, a biopsy performed at the appropriate stage would reveal no eosinophilia, and the diagnosis would be missed. Such being the case, the question arises as to how many cases remain undiagnosed or are regarded as Spiegler-Fendt sarcoid and other such vague expressions of leukotic disease. It is not clear whether the waves of eosinophilia coincide consistently with the regression of the lesions.

It is curious that the subject of eosinophilic granuloma of the skin should have been so suddenly introduced into dermatology in the United States. Probably the recent publicity for eosinophilic granuloma of bone is mostly responsible, but it still remains that the eosinophilia is so striking that it ought to have aroused comment years ago. The familiar

question in medicine at large now arises "Is this in fact a new disease, or has it simply been overlooked?" Only a laborious study of dermatologic histologic files can supply the answer. In any event, attention should be focused on newer factors in the life of the population which might be bearing an influence on its tissues, especially the hemopoietic ones. The sulfonamide drugs, barbiturates, aminopyrin and ethyl lead are in point. These are worth while covering when the clinical history is being elicited.

#### RELATIONSHIP TO EOSINOPHILIC GRANULOMA OF BONE, LOEFFLER'S SYNDROME AND THE SYPHILOID OF CATS

*Eosinophilic Granuloma of Bone* Lesions of the bone and skin in the same patient have been reported but once. Gross and Jacox<sup>7</sup> simply stated that their 4 year old patient with eosinophilic granuloma of bone had two small intracutaneous plaques in the left eyelid, but a cutaneous lesion apparently was not examined histologically and it is not known whether it was eosinophilic. It may have been a xanthoma. I agree with Lever and with Lewis and Cormia that there is not any proof at present that eosinophilic granuloma of bone is related to that of the skin. If there is any connection, it could be established only in a most roundabout way, i. e., through transitional forms of Letterer-Siwe and Hodgkin's diseases, such as was indicated by Dobes and Weidman. If this mechanism should obtain, it would occur within the idiopathic group of the cutaneous eosinophilic granulomas (containing Hodgkin's disease and other reticuloendothelioses).

*Loeffler's Syndrome* In Loeffler's syndrome, though, there are real possibilities of a relationship with eosinophilic granulomas of the skin. In connection with pulmonary symptoms which sometimes suggest tuberculosis, the roentgenologist has discovered transitory banal infiltrations in the lungs, and necropsy has demonstrated that they contain great number of eosinophils (von Meyerburg). Sometimes they affect an entire lobe. They are fleeting indeed, lasting but three to eight days. The eosinophilia of the blood ranges from 8 to 66 per cent. The journals of tropical medicine are outstanding in their reports of this disease because animal parasites (ranging from *Ascaris* to *Amoeba*) are the occasion for the eosinophilia; Hodes and Wood<sup>8</sup> called it "tropical eosinophilia." Indeed, the injection of extracts of *Ascaris* has proved the eosinophilogenous role of these parasites through the mechanism of allergy. The interstitial tissue (not the bronchi) is the shock

<sup>7</sup> Gross, P., and Jacox, H. W. Eosinophilic Granuloma and Certain Other Reticulo-Endothelial Hyperplasias of Bone, *Am J M Sc* **203** 673 (May) 1942

<sup>8</sup> Hodes, P. J., and Wood, F. C. Eosinophilic Lung (Tropical Eosinophilia) *Am J M Sc* **210** 288-295 (Sept) 1945

organ<sup>9</sup> However, animal parasites are not always demonstrable, notably in the cases in Palestine and those in which cutaneous manifestations were associated

Cutaneous involvement has been established by Lyon and Kleinhaus<sup>10</sup> They reported 20 cases in Jerusalem in six months, although several patients did not exhibit pulmonary lesions They cited other authors, who spoke of "eosinophilic erythroedema" and "eosinophilic disease with cutaneous manifestations" and of eosinophilia in the sternal bone marrow in addition to the other lesions Substantially, the dermatosis qualifies as a diffuse erythema multiforme perstans in large patches, affecting both the skin and the oral mucosa and often migrating It does not have any significant distribution The onset can be as sudden as in angioneurotic edema It is regrettable, to say the least, that a biopsy was not performed on a specimen of the skin, because it would serve as a base line for evaluation of the other eosinophilic granulomas of the skin Inasmuch as their publication may not be readily accessible, the following excerpt is supplied from their communication

Swelling of the skin develops somewhere partly heralded by prodromi, such as general malaise, desire for sleep, pain in the chest, abdomen or back, partly out of perfect health, usually without or only with insignificant elevation of temperature The skin over these areas may be oedematous but may also be red, hot, resembling urticaria or erysipelas, lymphangitis, or it may also appear in the shape of a boil The swollen areas may show great variation in size, distribution and localization Occasionally the same region is several times attacked The swelling may be diffuse, spreading over an entire arm but may also be small and irregular in shape There are itching, tension and pain of a varying degree A sensation of heaviness of the feet may render walking difficult, or may, if it appears in the arms, hinder the patient in his work A characteristic feature is the migratory character of the swellings which may persist from 2-8 days, or even longer In one case swelling of the arm continued to be present for almost seven weeks Only in one case was a subcutaneous nodule discovered in the skin of the shoulder Two cases presented swelling of the cervical lymph nodes, two swelling of the mucous membrane of the mouth persisting for a few days, and in one case there was oedema of the eyelid Part of the patients feel quite comfortable, others experience a certain discomfort and are unable to work

With only one exception, the blood contained an increased amount of eosinophils (7-50 per cent), there is further leucocytosis (8,000-15,000) The blood sedimentation is normal or slightly accelerated The red cell count is normal In our cases the migratory and recurrent swellings of the skin, accompanied by eosinophilia of the blood, persisted for several weeks, occasionally 2-3 months The affections is not dangerous but troublesome

9 Transitory Pulmonary Infiltrations Associated with Eosinophila (Loeffler's Syndrome), editorial, *J A M A* **126** 837 (Nov 25) 1944

10 Lyon, E, and Kleinhaus, E M An Eosinophilic Disease with Cutaneous Manifestations Associated with Transitory Pulmonary Infiltration (Loeffler's Syndrome), *Acta med orient* **4** 144-149 (May) 1945

This syndrome may be highly significant for the mechanism in the symptomatic group of eosinophilic granulomas of the skin such as I have outlined in previous pages. There is here a clearcut illustration of a proved specific agent (the animal parasite in some cases) which induces interstitial eosinophilic masses. Whether it occurs in a focus of preexistent congestion or bronchopneumonia remains to be demonstrated, but if such were the case (and it is possible) it would indicate by analogy that the eosinophilic infiltrations in the skin could develop through a similar pathologic mechanism. It would be illuminating indeed to study histologic sections of some of our typical dermatoses such as erythema nodosum and even tuberculosis and learn whether they too were unduly eosinophilic as they occurred in the tropics and in the presence of animal parasitic disease. Or would the experimental induction of eosinophilia in human beings or animals result in a histologic modification of preexisting dermatologic lesions in the direction of eosinophilia?

In any event, a new message has come to dermatologists. Patients with persisting erythema multiforme lesions (including migrating ones) demand study into the possibilities of Loeffler's syndrome. In the United States, animal parasites are not calculated to be demonstrated, but the experience in Palestine indicates that they are not a *sine qua non*.

*The Syphiloid of Cats* From the purely histologic viewpoint, the syphiloid of cats must be also regarded as one of the eosinophilic granulomas of the skin. Lever and also Lewis and Cormia supply adequate reasons for proving that it is neither etiologically nor clinically identical with the human cases described in the literature. However, to those who would insist that the concept of eosinophilic granuloma of the skin must comprehend a specific etiologic factor and a clinical picture that constitute an entity, the syphiloid of cats supplies the answer. It satisfies all the criteria for an entity—etiologic, clinical and histologic. By reason of priority, too, it would be the true eosinophilic granuloma of the skin. However, for practical purposes in human medicine, largely as the result of usage of the term, it appears to be advisable to include this lesser disease item within the larger and regard its eosinophilia as only an additional expression of the effects of one of the manifold etiologic agents (supposedly micro-organismal in this case) in the premises. Incidentally, an animal is at hand here for the experimental study of eosinophilic granuloma, and, inasmuch as several cases of eosinophilic granuloma of the skin have involved the lips, vulva or anus, the possibility of transmission from cats to human beings must not be forgotten. In fact, Pautrier stated in his discussion that Nanta and Gadrat's case was indistinguishable from the syphiloid of cats, the lesions were perianal and peribuccal.

## SIGNIFICANCE AND ROLE OF LIPIDS

In my personally studied cases, only two opportunities were supplied for testing for the presence of fat in the skin. Singularly, it was demonstrated in both cases, and it is recommended that such tests be conducted routinely in future cases of eosinophilic granuloma of the skin and also that the fat content of the blood be determined. Lever, alone, raised this subject, he found a few lipid-laden histiocytes and foam cells in his sections. The significance of this toward Letterer-Siwe disease has been discussed sufficiently elsewhere, but extreme caution must be exercised in view of the presence of fat glands in the skin which might have become disintegrated. In the sections that I studied, though, there was not any evidence of such disintegration.

## SUMMARY

The 10 European cases have been analyzed, the 20 cases occurring in Loeffler's syndrome and the syphiloid of cats have been discussed and sections have been examined by me in 9 American cases. They appear to fall into two groups pathologically, namely, the idiopathic and the symptomatic. A working classification is submitted on that basis, and it indicates also the widely divergent prognosis. Inasmuch as the disease is not an entity but only a histologic syndrome, "eosinophilic granulomas" is more fitting than "eosinophilic granuloma." "This is one of the eosinophilic granulomas of the skin" is a more proper statement when speaking of an individual case. The diagnosis can be made only histologically, sections are the first clue in diagnosis, but in view of the frequent plaquelike involvement of the face, it must be taken into account in the differential diagnosis of apparent sarcoid, leukemia, erythema elevatum diutinum and possibly lupus erythematosus. It is impossible to formulate blanket diagnostic formulas or prognoses to cover all cases of this disease.

Inasmuch as cutaneous manifestations appear in Loeffler's syndrome in the form of persistent erythema multiforme, it is in order (1) to determine whether sections of skin in this syndrome exhibit the features of eosinophilic granuloma and (2) to take note of the role of Loeffler's syndrome in dermatology. Eosinophilic granuloma of bone does not appear to be related to eosinophilic granuloma of the skin, but the demonstration of fat in cutaneous lesions opens the way for further inquiry through the avenue of Letterer-Siwe disease. The eosinophilic granuloma of cats (syphiloid) can be classified (histologically) among the eosinophilic granulomas of the skin at least temporarily.

The disease has appeared so abruptly in dermatology that attention should be paid to newer factors in the life of the population such as are calculated to induce eosinophilia (newer drugs and other agents).

In line with the ideas of Sulzberger<sup>11</sup> concerning histamine and allergy, the thesis is offered that the eosinophilic features are but additive to well known dermatologic entities such as erythema multiforme and Hodgkin's disease and that the eosinophilogenic factors may be responsible for obscuring and/or modifying the typical features of such entities. Of these factors, allergy stands in the forefront.

In the idiopathic group, eosinophilia of the blood (up to 72 per cent) is almost always present. The cellular infiltrate in the skin is far more polymorphous. The eosinophils vary in number at different stages of the disease, both in blood and in tissue, and one must be prepared for cases of eosinophilic granuloma of the skin *sine* eosinophilia.

11 Sulzberger, M. B. Year Book of Dermatology and Syphilology, Chicago, The Year Book Publishers, Inc., 1944.

## EOSINOPHILIC GRANULOMA

Theoretic and Practical Considerations Based on the Study of a Case

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A PATIENT with bizarre, recurrent, eosinophilic tumefactions of the skin has been under observation for the past three and one-half years. The clinical findings, in comparison to those noted in previous reports, are unique inasmuch as the individual lesions have been of relatively short duration with a tendency to spontaneous disappearance, are acutely inflammatory in nature and are completely insensitive to irradiation with roentgen rays.

As a background for discussion of this case, the pertinent literature will first be summarized. Following the presentation of the case, an attempt will be made to link up the various eosinophilic tumefactions into a logical pattern and to clarify the relationship between these lesions and eosinophilia in general.

### SUMMARY OF ANALOGOUS CASES

The first case of cutaneous eosinophilic granuloma to be reported was that of Freund<sup>1</sup> in 1930. His patient had active pulmonary tuberculosis. For six years there were present livid red, semicircular infiltrations on the eyelids, hard, verrucoid and hyperpigmented nodules on the arms and legs, and a cordlike lesion on the right cheek and jaw. There was no significant adenopathy. Trichophytin test and serologic tests of the blood elicited negative reactions, while a blood eosinophilia of 22 per cent was present. Studies of biopsy specimens revealed a slight acanthosis and a vasodilatation and edema of the papillae. Throughout the cutis and extending to the subcutaneous tissues was a widespread, dense infiltrate, which had caused extensive destruction of connective tissue fibers, hair follicles and sebaceous glands. The infiltrate was predominantly eosinophilic, with, in addition, some lymphocytes,

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<sup>1</sup> Freund, E. Su un caso di strani tumori cutanei in una tubercolosa, *Dermosifilograf* 5 617 (Oct) 1930.

monocytes, histiocytes, plasma cells, mast cells, giant cells and epithelioid cells. The blood vessels were the seat of extensive endarteritis with hyaline degeneration of the intima and adventitia. The lesions improved greatly after roentgen ray therapy, but the patient was lost from observation and the end result was not known. Freund stated the belief that the granuloma might represent an atypical form of mycosis fungoides or Hodgkin's disease.

Pasini's case,<sup>2</sup> properly labeled as eosinophilic granuloma, was the second example of the syndrome to be reported. The patient was a woman of 69 years, with long-standing nonulcerated tumefactions of the forehead, left side of the face and left mandibular region. The onset had been eight years before, with a nodule which slowly extended peripherally, with the formation eventually of an irregularly surfaced hemispheric area 5 by 7.5 cm. The lesions on the left side of the face began as three separate nodules, with gradual extension and coalescence over the side of the face and mandibular region. Slight pruritus was occasionally noted. The lesions were bluish red, were elastic to firm in consistency and presented considerable nodule-like irregularities of the surface. The peripheral borders were raised and indented, while the central areas were depressed and atrophic, ulceration never developed. There were no systemic symptoms or evidence of impaired general health. Physical examination, serologic tests of the blood for syphilis and roentgenograms of the skull, thorax, hands and feet gave normal results. The hemogram was normal with the exception of a white blood cell count of 11,600, the increase in cells presumably being due to eosinophils (41 per cent). Histopathologically, there were moderate atrophy of the epidermis and absence of interpapillary pegs. The principal abnormality was a compact dermal infiltrate extending from the subpapillary zone throughout the deeper cutis and at times to the subcutaneous fatty tissue. There was almost complete destruction of the normal elements of the connective tissue and the sweat glands. The infiltrate consisted of great numbers of eosinophils (either mononuclear or polymorphonuclear), with, in addition, considerable small and large lymphocytes, histiocytes and fibroblastic proliferation. There were a few plasma and mast cells but no giant cells. The smaller blood vessels were increased in number and were the seat of an extensive endarteritic thickening. Edema of the tissues was not present. Roentgenologic irradiation was given, with considerable improvement, but the end result was not stated.

Martinotti<sup>3</sup> recorded briefly 3 cases of "eosinophilic" granuloma, but of these only 1 seems to fit into the group of specific eosinophilic

2 Pasini, A. Granuloma eosinofilo, *Gior. ital. di dermat. e sif.* **81** 1 (Feb.) 1940.

3 Martinotti, L. Granuloma eosinophilum, *Dermat. Wchnschr.* **112** 25 (Jan. 11) 1941.

tumefactions. This patient was a soldier who had chronic, infiltrated and at times ulcerated plaques on the legs. On section, the infiltrate was found to be mainly eosinophilic, with some mast cells, plasma cells and fibroblastic proliferation. Cure was obtained by surgical excision.

Cerutti<sup>4</sup> has made the most recent report of this rare syndrome. His patient was a woman, aged 41, in whom during the preceding three months there had developed a nodular and noduloulcerative eruption. The lesions consisted of doughy to firm, reddish brown tumors, some with necrotic tops. The distribution was widespread, with a tendency to seborrheic localization, the scalp, hands and feet were spared. There was no lymphadenopathy except for a large cervical lymph node on the left side. A blood eosinophilia of 47 per cent was recorded. Histopathologic studies revealed (1) a lymphosarcomatous tumor of the cervical lymph nodes on the left side and (2) a granuloma, predominantly eosinophilic in type, involving the skin. In the cutaneous lesions a compact infiltrate involved the entire cutis. When the epidermis was not specifically invaded, there was an overlying acanthosis and spongiosis. In some areas, however, the epidermis was massively infiltrated with cellular elements from the granuloma in the cutis, and in these areas necrosis frequently supervened. The infiltrate in the cutis was massive and more or less completely replaced the normal structures. The cells were largely eosinophilic in type (both mononuclear and polymorphonuclear) and occurred both diffusely and in perivascular localizations. A few lymphocytes, epithelioid cells and histiocytes were also present. Cerutti noted that in peripheral zones histiocytes with acidophilic granules were present and expressed the opinion that these cells might be the precursors of tissue eosinophils. As in the cases of Freund and Pacini, the blood vessels were the seat of an extensive endarteritis and thickening, but the possible significance of this phenomenon was not discussed. The patient was given roentgen ray therapy, which effected a dramatic and permanent improvement in the eosinophilic tumors. The sarcoma, on the contrary, was unaffected, continued to spread and finally resulted in the death of the patient by its metastases. The progression of the sarcoma was not accompanied with a relapse of the cutaneous lesions, and Cerutti was of the opinion that the two diseases were unrelated.

#### OTHER EOSINOPHILIC TUMORS OF THE SKIN

The concept of a cutaneous eosinophilic granuloma as a well defined clinical entity has been complicated by the recent reports of cases by Pautrier,<sup>5</sup> Nanta and Gadrat,<sup>6</sup> Lapiere<sup>7</sup> and Lefevre and his associates.<sup>8</sup>

4 Cerutti, P. Il granuloma eosinofilo, *Dermatologica* 85:90, 1942.

The cases of Lefevre and his co-workers and of Lapière will be discarded from further consideration as probable examples of lymphoblastoma of unknown type and Hodgkin's disease respectively. The patients described by Pautrier and by Nanta and Gadiat, while clinically distinct from the present case, had lesions which on histopathologic study showed a predominantly eosinophilic type of infiltrate, and for this reason they will be reviewed.

Pautrier's patient was a man aged 25 who had a perianal and rectal granuloma of one and a half years' duration. The lesions were verrucous and vegetating and extended from the primary location to the adjacent surface of the buttocks, the anal wall and for several centimeters along one side of the rectal mucosa. The patient had a partially treated syphilitic infection and had suffered previously from amebic dysentery. There was no clinical resemblance to lymphogranuloma venereum, however, the Frei test elicited a weakly positive reaction. Studies of a biopsy specimen revealed a decided verrucoid acanthosis and a dense infiltrate throughout the cutis. This infiltrate was composed of lymphocytes, plasma cells, small histiocytes and moderate numbers of eosinophils. Scattered polymorphonuclear cells and small zones of necrosis were noted.

The patient of Nanta and Gadiat was a man aged 21 who had diabetes insipidus, pleurisy and active pulmonary tuberculosis. Diffuse tumefactions developed on the lower gingiva and a vegetating granuloma in the perianal region and the distal part of the rectal mucosa. Histopathologic changes included a moderate acanthosis and a dense infiltrate throughout the cutis, predominantly eosinophilic, with, in addition, some histiocytes, monocytes, plasma cells and mast cells.

It is noteworthy for both patients that the striking endarteritis and subsequent vascular thickening noted in the patients of Freund, Pacini and Cerutti and in the case to be presented were conspicuous by their absence. The pronounced epidermal changes were probably indicative of a more "toxic" form of tissue reaction, moreover, blood eosinophilia was not a feature. It would seem that an entirely different type of pathologic tissue reaction was taking place, with such obvious etiologic

5 Pautrier, L. M. Le granulome eosinophilique, Bull Acad de med de Roumanie **3** 432, 1938.

6 Nanta, A., and Gadrat, J. Sur un granulome eosinophilique cutané, Bull Soc franç de dermat et syph (Reunion dermat, Strasbourg) **44** 1470 (July) 1937.

7 Lapiere. Un cas de granulome éosinophilique, Bull Soc franç de dermat et syph (Reunion dermat, Strasbourg) **44** 1479 (July) 1937.

8 Lefevre, P., Coirre, and Levy-Coblentz, G. Granulomatose cutanée a evolution febrile avec eosinophilie sanguine à 46% sans determinations ganglionnaires, Bull Soc franç de dermat et syph (Reunion dermat, Strasbourg) **44** 1604 (July) 1937.

possibilities as cutaneous amebiasis, tuberculosis and lymphogranuloma venereum to be strongly considered

It would seem that the cases both of Pautrier and of Nanta and Gadrat bore superficial resemblances to the so-called syphiloid of the cat, recently described by Henry and Bory<sup>9</sup> However, in this ill defined entity, the sites of involvement are different Chancriform lesions are present on the lip and hypertrophic plaques in the inguinocrural and perianal regions Moreover, a satellite or distal lymphadenitis is often a prominent feature Lastly, the cellular infiltrate, while somewhat similar to that seen in eosinophilic granuloma, is unaccompanied with significant changes in the blood vessels

#### REPORT OF A CASE

M R, a Jewish-American man of 47, was first seen three and one-half years ago because of recurrent, moderately pruritic tumefactions involving the trunk and extremities He was presented at the Manhattan Dermatologic Society in October 1942 (A Case for Diagnosis [Erythema Nodosum?], ARCH DERMAT & SYPH 48 436 [Oct] 1943) and at the New York Academy of Medicine, Section on Dermatology and Syphilis, in May 1943 (A Case for Diagnosis [Eosinophilic Granuloma?] ARCH DERMAT & SYPH 49 375 [May] 1944)

The family history was unremarkable, there being no constitutional or allergic diseases and no serious infections The patient has shown some increased susceptibility to infections Because of recurrent tonsillitis, tonsillectomies were performed at the ages of 12, 13, 14 and 25 Five abscessed teeth were extracted between the ages of 19 and 30, at the latter time fourteen additional teeth, all with abscesses, were removed He then began to experience severe headaches and during the ten years intervening up to the onset of the present trouble took large doses of acetylsalicylic acid and other coal tar derivatives A chronic dermatophytosis of the soles and interdigital areas of the feet has been present for at least seven years Vesiculation or other acute inflammatory changes have never occurred, and dermatophytid has not ensued There was, moreover, no increase in the severity of the dermatophytosis just prior to the onset of the chief complaint

The present cutaneous disease began six years ago on the inner aspect of the left thigh, as a small, firm, pinkish papule Independent satellite lesions were soon noted, all areas enlarged peripherally and formed a large, deep, soft, pendulous sac, with evidence of edema shown by a pigskin-like surface The color was initially pinkish red, became a darker red after seven to ten days and then gradually faded out as the lesions disappeared during the following two weeks Involution has always been followed by a moderate degree of residual hyperpigmentation Four of these tumefactions made their appearance on the thighs during the first four months of the disease, following which there was a six month period of freedom Recurrences were then noted, this time involving both the arms and the thighs The evolution of the lesions, while similar in pattern, became much slower, and nine to ten weeks were required for the complete cycle The lesions were initially gyrate in configuration, later becoming deep, hard, solid plaques which

9 Henry, A, and Bory, L La syphiloïde du chat (granulome eosinophilique), Bull Soc franç de dermat et syph (Reunion dermat, Strasbourg) 44 1486 (July) 1937

eventually softened and cleared from within outward. Furthermore, during the height of the multiple plaque formation, the entire lower extremities became swollen to one-half greater than normal size. During the next two years, the

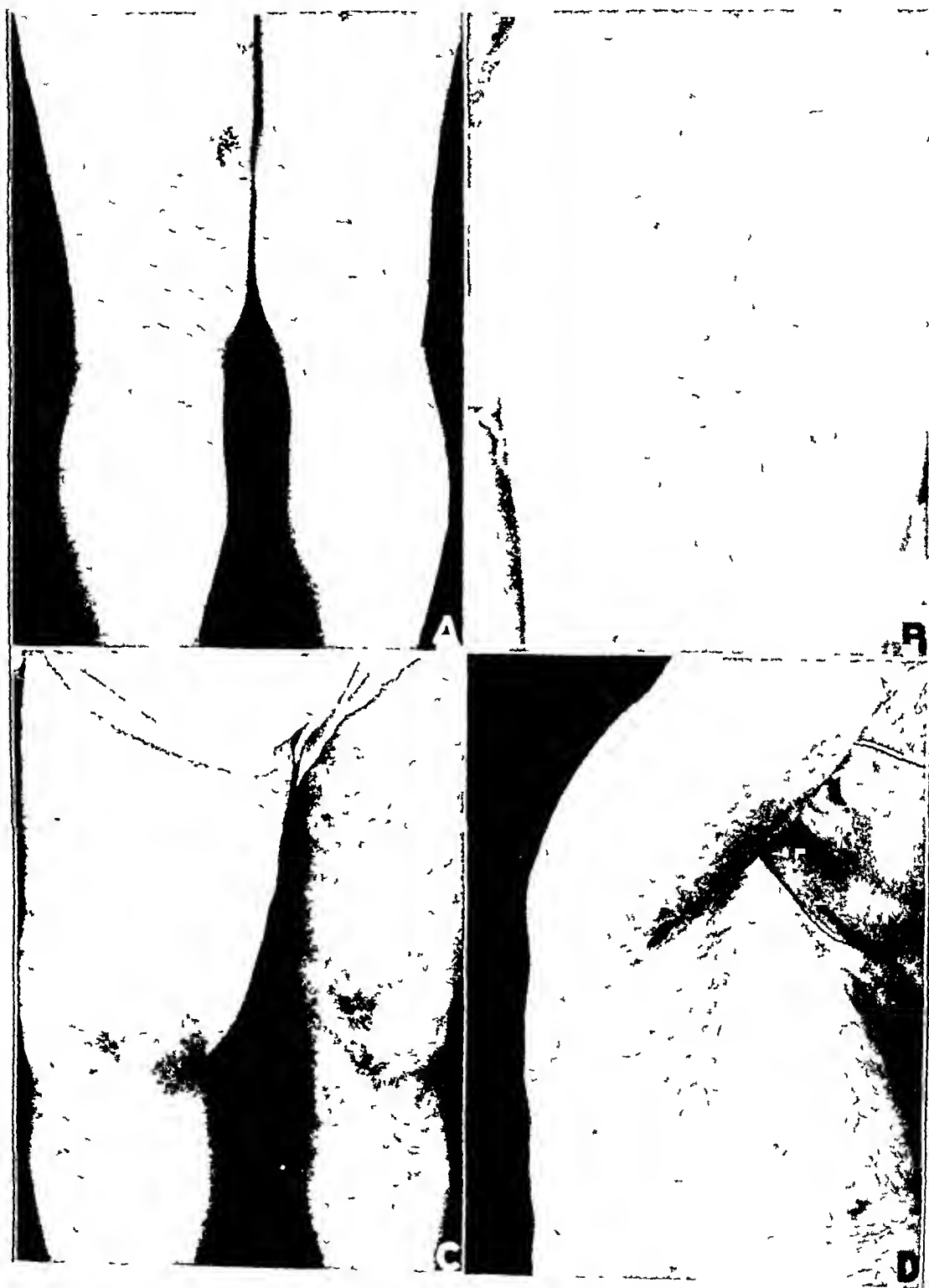


Fig 1—Lesions of eosinophilic granuloma at various stages of evolution. *A*, early lesions. *B*, plaquelike tumefaction due to peripheral enlargement. *C*, massive edema at height of process and *D*, spreading process with solitary and plaquelike lesions.

body became increasingly involved by the process and even the soles were affected. The scalp, face and neck have been consistently free. The plaque-like character of the lesions has continued to date, the diffuse swelling, on the contrary, abated after another year and has been absent in the last three years to date. Lesions have been absent only for brief periods during the past five years, but there has been a gradual decrease in severity of attacks in the last two years. Ulceration has never occurred.

The attacks are invariably preceded by severe burning urination, increased frequency and polyuria. The tumefactions are accompanied throughout their course with a moderate pruritus, which is difficult to relieve by either local or systemic therapy. Local trauma has apparently resulted in the development of new lesions, but only in periods when lesions are spontaneously occurring. Treatment of the



Fig 2—Early lesion, showing beginning vascular and perivascular changes

accompanying dermatophytosis with ointment of benzoic and salicylic acid during periods of remission has resulted in a new severe attack on three occasions. Increase in size is thought to result from aggravation from nervous tension, but the attacks are never initiated in this fashion.

Extensive laboratory investigations were made three and one-half years before this paper was written and have been made at various intervals to date. Significant positive results were as follows: (1) isolation of *Trichophyton purpureum* from the dermatophytosis of the feet, (2) strongly positive immediate and delayed trichophytin reaction, with a central wheal of 2 cm and a surrounding erythema of 4 to 5 cm, (3) blood eosinophilia varying from 5 to 13 per cent, and (4) bone marrow eosinophilia of 15 per cent. Significant negative results included normal findings in urinalyses, roentgenograms of the chest, blood cultures, sedimentation rate, tuberculin test, prostatic culture and an extensive series of intradermal tests with pollens, dusts, feathers, various animal extracts, foods,orris root, pyrethrum

flaxseed, silk, tobacco, trees, timothy and ragweed. Examination of the stool did not reveal parasites, and cultures of several biopsy specimens of the skin were negative for pathogenic bacteria and fungi. The Kline and Kahn tests of the blood elicited negative reactions.

During the period of observation some twenty biopsy specimens were examined. Specimens were taken from lesions at various stages in their evolution, and it was possible therefore to reconstruct to some degree the sequence and pattern of the pathologic changes. The significant abnormalities occurred only in the cutis. The epidermal changes were purely secondary in nature, in early lesions the epidermis was normal, later a slight acanthosis was variably present, while lesions which had undergone involution contained a moderate increase in melanin pigmentation in the basal layer.

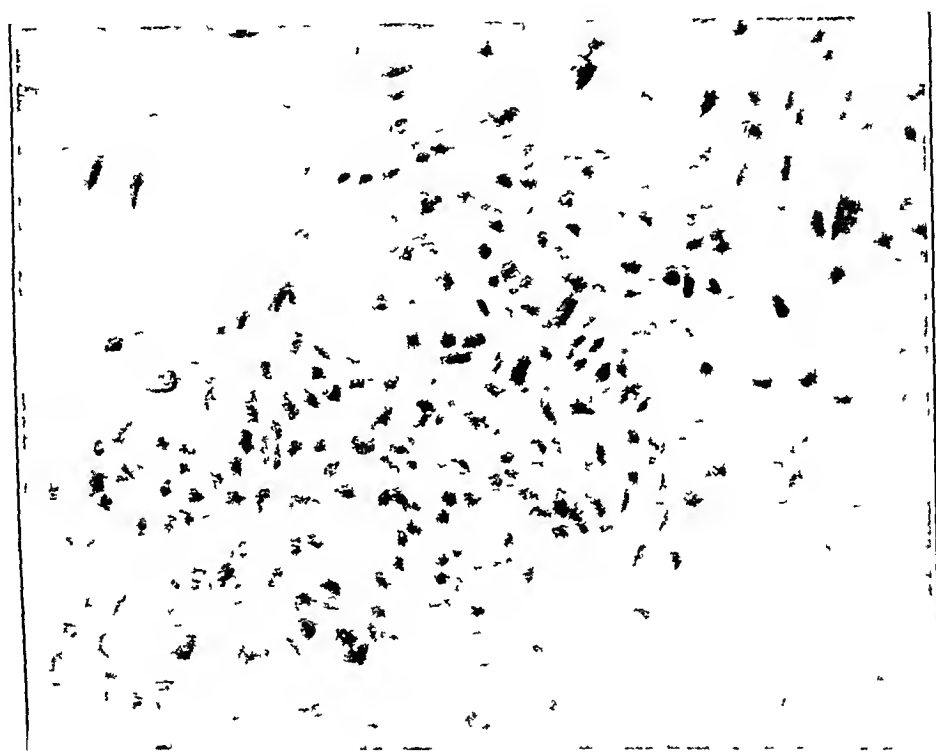


Fig 3—More pronounced early lesion, with endarteritis, dilatation of the lymphatic vessels and pleomorphic infiltrate.

The earliest demonstrable pathologic lesion was a mild dilatation of the smaller blood vessels of the subpapillary zone and the mid cutis, with some swelling of the endothelial cells and adherence of blood-borne leukocytes to the lumens. These dilated vessels were surrounded by a sparse infiltrate composed mainly of small lymphocytes and a few histiocytes.

As the evolution of the lesions continued, beginning endarteritis and thickening of the small blood vessels could be noted. The perivascular infiltrate became more pronounced and more pleomorphic in character, with lymphocytes, histiocytes, plasma cells and a few mononuclear eosinophils. The perivascular lymphatic vessels showed considerable engorgement.

In a moderately advanced lesion, the infiltrate became more compact and could be noted throughout the middle and deeper portions of the cutis. It still showed a tendency to a perivascular distribution with a dense encroachment on blood

vessels that were the seat of decided endarteritis and thickening. It also occurred around sweat ducts, hair follicles and sebaceous glands. While the pleomorphic type of infiltrate remained, increasing numbers of mononuclear and polymorphonuclear eosinophils could be observed. Moderate edema of the tissue had now supervened.

In a fully developed lesion the infiltrate was almost solidly present throughout the mid portion and deeper portions of the cutis, while in some sections it had even invaded the subcutaneous adipose tissue.

Much of the normal connective tissue was replaced by the dense masses of cells, while the entire section showed a rather decided edema. The blood vessels were extensively thickened, in some instances with diminished lumens and in others with complete obliteration of the lumen. The infiltrate, while retaining

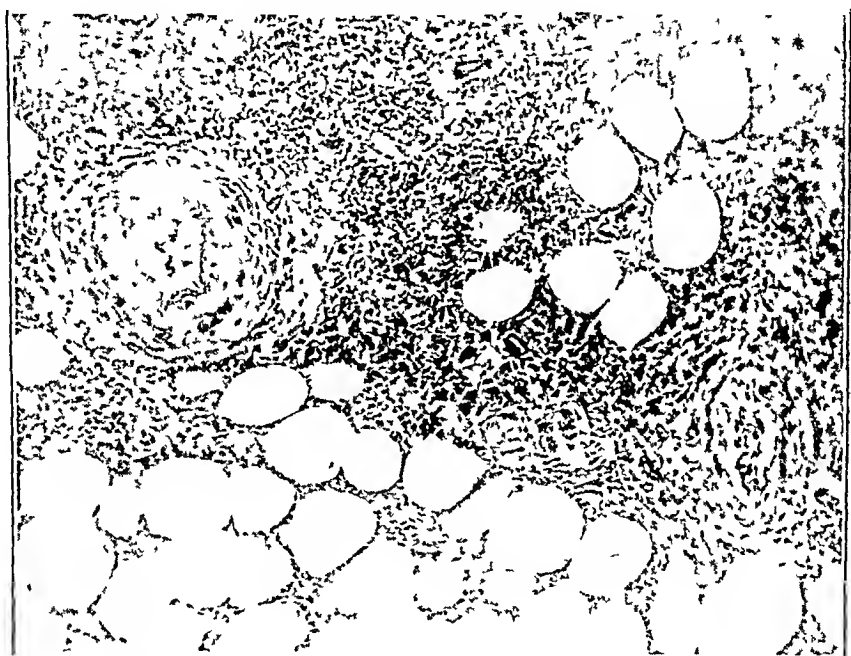


Fig 4—The fully developed lesion shows extensive endarteritis and massive eosinophilic invasion of the deep cutis.

its polymorphous character, contained a great increase in percentage of mononuclear and polymorphonuclear eosinophils. The eosinophils were seen throughout the granuloma. However, they tended to be concentrated along the outer walls of the blood vessels. In some areas eosinophils were noted lying free along the collagen fibers, and eosinophilic granules could be seen extracellularly in the tissue.

As the lesions receded, the infiltrate became less eosinophilic in character and lymphoblasts, histiocytes and small leukocytes were more numerous. A striking feature was observed in a biopsy specimen taken two years after clinical involution of the lesion had occurred. In this section eosinophils, histiocytes and plasma cells were absent, and only a sparse perivascular infiltrate of small lymphocytes was present. The blood vessels, however, still showed a considerable amount of endarteritic thickening of a regressive type. Corresponding to the residual hyper-

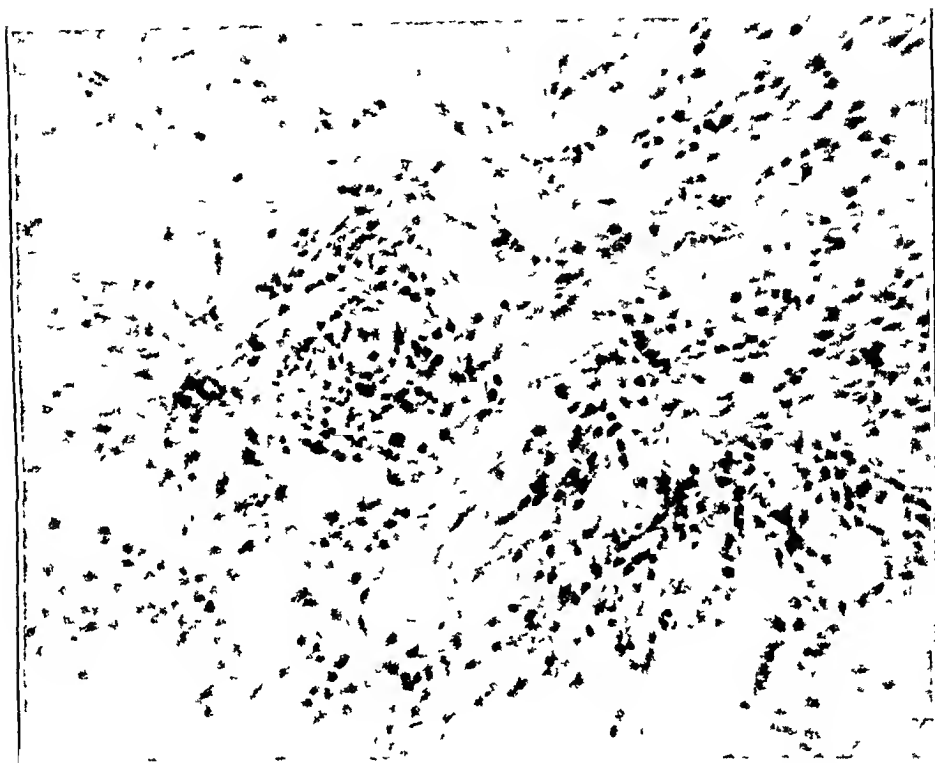


Fig 5—Advanced lesion, showing eosinophilic infiltrate occurring perivascularly and along collagen fibers

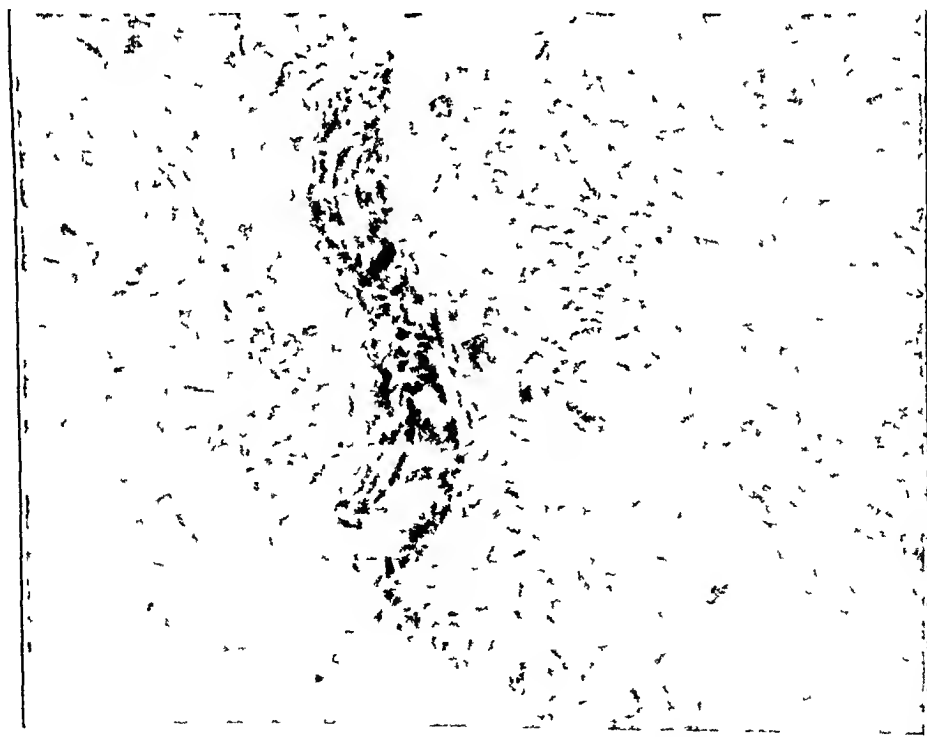


Fig 6—Lesions which have undergone involution, showing hyperpigmentation, residual endarteritis and perivascular infiltration

pigmentation noted clinically, appreciable amounts of melanin were present in the deeper layers of the epidermis

The clinical progress of the lesions was but slightly modified by therapy. Roentgen irradiation was entirely without effect, while various topical remedies were of but minor palliative value. Two courses of potassium iodide by mouth were administered. There was no improvement during the first course, but the second course, which continued for eight months, with the eventual establishment of a daily dose of 280 grains (15.8 Gm.), effected a 30 per cent amelioration in the severity of the lesions. It is interesting also that an injection of trichophytin two years previous to the writing of this paper was followed by a clinical exacerbation. Recently, eight intradermal injections of trichophytin and histamine at weekly intervals were administered. This treatment resulted in no demonstrable improvement of the disease, on the contrary, the customary involution of the lesions was delayed, and finally a striking exacerbation occurred, so the therapy was discontinued.

#### EOSINOPHILIC GRANULOMAS IN OTHER BODY STRUCTURES

Other tissues and organs may be the sites of granulomatous tumors somewhat comparable to those seen in the skin. Specifically, the bones,<sup>10</sup> the lungs,<sup>11</sup> and the reticuloendothelial system<sup>12</sup> have been reported to be involved.

The bone lesions, first reported by Mignon,<sup>10</sup> may be solitary or multiple, affecting frequently the skull and occurring commonly in childhood and adolescence. The tumefactions are reported to follow trauma frequently. Specific allergic factors have not been determined. Pathologically, the granulomas are composed of compact masses of large histiocytes associated with mature and immature eosinophils. Polymorphonuclear, plasma and giant cells are occasionally seen. As the disease progresses, foam cells and an increased amount of lipid may be present. Replacement of connective tissue finally makes way for transformation back to bone.<sup>13</sup> Roentgenographically and at times pathologically, the lesions of eosinophilic granuloma of bone are indistinguishable from Hand-Schuller-Christian disease involving bone.<sup>14</sup> Frequently, there is an associated blood eosinophilia of 5 to 10 per cent. The lesions may disappear spontaneously or be cured by roentgen therapy or surgical excision.

10 Mignon, F. Ein Granulationstumor des Stirrbeins, *Fortschr. d. Geb. d. Röntgenstrahlen* **42** 749 (Dec.) 1930.

11 Löffler, W. Die flüchtigen Lungeninfiltrate mit Eosinophilie, *Schweiz. med. Wchnschr.* **66** 1069 (Nov. 7) 1936.

12 Jaffe, H., and Lichtenstein, L. Eosinophilic Granuloma of Bone, *Arch. Path.* **37** 99 (Feb.) 1944.

13 Green, W., and Farber, S. Eosinophilic or Solitary Granuloma of Bone, *J. Bone & Joint Surg.* **24** 499 (July) 1942.

14 Mallory, T. Medical Progress Pathology. Diseases of Bone, *New England J. Med.* **227** 955 (Dec. 17) 1942.

The pulmonary syndrome, first described by Löffler,<sup>15</sup> occurs as transient pulmonary infiltrations, often recurrent, accompanied with cough, mild fever and symptoms of asthma. There is a mild leukocytosis with a blood eosinophilia of 10 to 50 per cent and a high bone marrow eosinophilia.<sup>16</sup> The disease is reputedly not fatal, so that it is interesting and noteworthy that von Meyenburg<sup>16</sup> described the pathologic anatomy of the pulmonary lesions in 3 subjects, all of whom died accidentally in Nazi Germany in 1942. According to von Meyenburg the lesions consist of an exudative inflammatory process accompanied with an infiltrate composed largely of eosinophils. A few lymphocytes, polymorphonuclear cells, plasma cells and giant cells are variably present and often perivascular in location. In some districts areas of thrombophlebitis and of necrosis have been found, but endarteritis was not described.

Specific allergenic factors such as amebas, intestinal worms, plants and pollens have been identified as causative agents in several cases,<sup>17</sup> and the elimination of these agents has resulted in permanent cure.

In cases reported to involve the reticuloendothelial system, the evidence is less convincing. In the syndrome described by Letterer<sup>18</sup> and Siwe<sup>19</sup> there develops during the first year of life a widespread histiocytosis involving the reticuloendothelial system, in which the bone marrow, liver, spleen, lymph nodes, alimentary tract, thymus and skin may be affected. The disease is invariably fatal when it develops in early infancy and becomes more benign, with chronicity the rule, when the onset is after the age of 2. Histologically the tumor cells consist of histiocytes, lymphocytes, plasma cells and eosinophils. At times the eosinophils may predominate. It has been reported that Hand-Schüller-Christian disease may supervene after a patient has reached the age of 2, becoming more typical by the fourth year of life.<sup>14</sup> Because of this reported transition to a probably unrelated disease and because of the absence of any significant allergic factors, the resemblance of the Letterer-Siwe syndrome to eosinophilic granuloma may be more apparent than real.

15 Löffler, W. (A) Zur Differential-Diagnose der Lungeninfiltrationen, (B) Ueber fluchtige Succedan-Infiltrate mit Eosinophilie, Beitr z Klin d Tuberk **79** 338, 1932.

16 von Meyenburg, H. Das eosinophile Lungeninfiltrat. Pathologische Anatomie und Pathogenese, Schweiz med Wchnschr **72** 809 (July 25) 1942.

17 Jones, S, and Souders, C. Eosinophilic Infiltration of the Lungs (Löffler's Syndrome), New England J Med **231** 356 (Sept 7) 1944.

18 Letterer E. Aleukamische Retikuloose, Frankfurt Ztschr f Path **30** 377, 1924.

19 Siwe, S. Die Reticuloendotheliose—ein neues Krankheitsbild unter den Hepatosplenomegalien, Ztschr f Kinderh **55** 212, 1933.

## COMPARABLE TISSUE REACTIONS

A critical analysis of repeated biopsy material suggests that the fundamental evolutionary features of the disease are (1) involvement of the smaller blood vessels of the skin, with dilatation and adherence of leukocytes to their endothelial surface, (2) beginning endarteritis and thickening of the vessels, with dilatation of the perivascular lymph spaces and an infiltrate which is at first lymphocytic but later becomes predominantly eosinophilic, (3) development of pleomorphism of the infiltrate, (4) more diffuse distribution of the eosinophilic infiltration and widespread edema, (5) gradual resorption of the infiltration and (6) the end stage of residual endarteritis and hyperpigmentation

In the cases reported by Freund, Pasini and Cerutti, the histopathologic features were essentially similar, although the evolution of the pathologic lesions was not clearly defined

In the cases described by Pautrier and by Nanta and Gadrat, the infiltrate was comparable but there was no evidence of a primary disturbance of the blood vessels

The infiltrate noted in the osseous and pulmonary lesions is of comparable nature, but the absence of stated vascular changes prohibits any further analogy

There would appear to be a striking similarity between the pathologic findings of periarteritis nodosa and eosinophilic granuloma of the skin, for in both diseases there is an initial involvement of the walls of the blood vessels and a subsequent pleomorphic infiltration in the perivascular tissues. In the first-named disease there is a more profound reaction in the arteries, with necrosis of the medium, obstruction and thrombosis of the lumen and subsequent infarction. The infiltrate, while similar to eosinophilic granuloma, is more localized. Furthermore, the disease may be widespread throughout the body. Recent observations<sup>20</sup> have suggested that in many, if not the majority of, instances the disease may be self limited, healing with residual fibrosis

DEVELOPMENT OF EOSINOPHILIA EXPERIMENTAL OBSERVATIONS  
BY OTHERS

From a consideration of experimental studies regarding the behavior and development of eosinophils, these cells have been shown to appear in the blood and/or tissues after exposure to the following substances (1) injection in animals of foreign protein in the form of specific or

20 Rich, A. The Role of Hypersensitivity in Periarteritis Nodosa as Indicated by Seven Cases Developing During Serum Sickness and Sulfonamide Therapy, *Bull Johns Hopkins Hosp* 71 123 (Sept) 1942

nonspecific antigens,<sup>21</sup> (2) injection of suspension in isotonic solution of sodium chloride of ground ascaris<sup>22</sup> in guinea pigs, (3) intramuscular injections of foreign proteins in human beings,<sup>23</sup> (4) sensitization by haptene antigens (phenylethylhydantoin or sulfonamide drugs<sup>21</sup>) and (5) in tissue cultures in presence of circulating antibodies<sup>25</sup>

The consensus is that the eosinophils are produced only in the bone marrow,<sup>26</sup> as first postulated by Ehrlich,<sup>27</sup> although some authors<sup>28</sup> hold that they may arise in local tissues as well

#### DISEASES IN WHICH EOSINOPHILIA IS A FEATURE

Eosinophilia is a feature in the following diseases (1) pruriginous diseases of the skin with repeated excoriations (dermatitis herpetiformis, lymphoblastomas such as mycosis fungoides, prurigo and atopic eczema<sup>28</sup>), (2) diseases of the skin with excessive destruction of tissue (pemphigus)<sup>28</sup>, (3) blood dyscrasias (Hodgkin's disease and eosinophilic leukemia, myelogenous leukemia and familial eosinophilia<sup>29</sup>), (4) intestinal parasites and trichinosis<sup>26</sup>, (5) allergic diseases (urticaria and asthma), (6) diseases probably of allergic nature (periarteritis nodosa<sup>29</sup> and Löffler's syndrome<sup>31</sup>), (7) drug reactions, including those due to phenylethylhydantoin, benzene and digitalis,<sup>29</sup> and (8) miscellaneous diseases and states (splenomegaly, splenectomy, polymyositis, ingestion of raw liver, ultraviolet irradiation and ionogenic irradiation<sup>30</sup>)

21 (a) Schlecht, H, and Schwenker, G Ueber locale Eosinophilie in den Bronchien und der Lunge beim anaphylaktischen Meerschweinchen, Arch f exper Path u Pharmakol 68 163, 1912 (b) Biggart, J Some Observations on Eosinophile Cell, J Path & Bact 35 799 (Sept) 1932

22 Herrick, W Experimental Eosinophilia with an Extract of an Animal Parasite Its Relation to Anaphylaxis and Certain Clinical Problems, Arch Int Med 11 165 (Feb) 1913

23 (a) Biggart<sup>21b</sup> (b) Peshkin, M M, and Messer, W Asthma in Children XII Influence of Specific and Nonspecific Treatment on the Differential Leukocyte Count, with Special Reference to the Eosinophils, Am J Dis Child 50 1374 (Dec) 1935

24 Landsteiner, K Serological and Allergic Reactions with Simple Chemical Compounds, New England J Med 215 1199 (Dec 24) 1936 Rich<sup>20</sup>

25 Haughton, B, cited by Kirk<sup>26</sup>

26 Kirk, R C The Causes of Eosinophilia, Internat Clin 1 219 (March) 1942

27 Ehrlich, P Methodologische Beiträge zur Physiologie und Pathologie der verschiedenen Formen der Leukocyten, Ztschr f klin Med 1:553, 1879-1880

28 Burkhart, R, and Montgomery, H Dermatologic Significance of Tissue Eosinophilia, Arch Dermat & Syph 49 19 (Jan) 1944

29 Lebowich, J, and Hunt, H Eosinophilia Diagnostic Significance in Periarteritis Nodosa, Am J Clin Path 10 642 (Sept) 1940

(Footnotes continued on next page)

## FUNCTION OF THE EOSINOPHILS

At the present time, the exact function is unknown. From the previously mentioned experimental work and listed diseases in which eosinophilia is noted in human beings, it would seem that eosinophilia develops as a result of destruction of body tissues or as a reaction to some protein or haptene antigen. Weinberg and Seguin have shown that eosinophils are phagocytic for bacteria, trichinella and peptone.<sup>31</sup> In addition, Code<sup>32</sup> has demonstrated that the histamine content of the blood is high in patients with eosinophilia. This raises the question whether eosinophilia and increased blood histamine are adventitious findings produced by a single factor or whether the eosinophils appear as the result of stimulation by histamine. The suggestion has been made that the eosinophilic granules have a high concentration of histamine, possibly as a protective mechanism.<sup>26</sup>

## SPECIFIC ETIOLOGIC CONSIDERATIONS

Examination of the reports of cases of previous examples of eosinophilic granuloma does not reveal a single instance in which a cause was determined. While the cause in the present case has not been finally proved, the following findings are of interest:

1 There was repeated demonstration of a *T. purpureum* infection of the feet.

2 Both immediate and delayed cutaneous hypersensitivity to trichophytin was present.

3 Vigorous treatment of the dermatophytosis resulted in definite exacerbation of the eosinophilic granulomas on three occasions.

4 During a series of intracutaneous trichophytin injections, there was a pronounced delay in the involution of the existing granulomas in comparison with previous attacks.

5 A widespread exacerbation of the disease developed two hours following an injection of trichophytin.

30 Goldsmith, W. N. *Recent Advances in Dermatology*, Philadelphia, P. Blakiston's Son & Co., 1936, p. 440. Minot, G., and Spurling, R. Effect on Blood of Irradiation, Especially Short Wave Length Roentgen-Ray Therapy, *Am. J. M. Sc.* **168**: 215 (Aug.) 1924. Kirk<sup>26</sup>

31 Weinberg, M., and Seguin, P. Recherches biologiques sur l'eosinophilie, proprietes phagocytaires et absorption du produits vermineux, *Ann. Inst. Pasteur* **29**: 323, 1915.

32 (a) Code, C. Source in Blood of Histamine-like Constituent, *J. Physiol.* **90**: 349 (Aug. 17) 1937. (b) Code, C., and Hester, H. Blood Histamine During Anaphylactic Shock in Horse and Calf, *Am. J. Physiol.* **127**: 71 (Aug.) 1939. (c) Code, C. Histamine Content of Blood of Guinea Pigs and Dogs During Anaphylactic Shock, *ibid.* **127**: 78 (Aug.) 1939.

6 Typical eosinophilic granulomas appeared at the site of several of the trichophytin injections, whereas none appeared at control sites

7 There was an absence of any other explanation for the disease.

8 Intensive and prolonged internal iodide therapy resulted in moderate clinical improvement

#### SUMMARY

1 A patient with frequently recurring pruritic edematous tumefactions of the skin has been studied for the past three and one-half years

2 The disease was characterized pathologically by endarteritis, followed by a predominantly eosinophilic infiltration

3 Evidence is submitted suggesting a relationship with a coexisting fungous infection of the feet (*T. purpureum*)

4 Reports of cases of eosinophilic granuloma of the skin, bones, lungs and reticuloendothelial system have been reviewed

5 The theories concerning the development and function of eosinophils have been considered

6 Since the initial and fundamental pathologic change of the skin is apparently in the blood vessels, the name eosinophilic perivascularitis would seem preferable to eosinophilic granuloma

66 East Sixty-Sixth Street

#### ABSTRACT OF DISCUSSION

DR UDO J. WILF, Ann Arbor, Mich.—I should like to report and to demonstrate another case of eosinophilic granuloma which was recently presented at a meeting of the Central States Dermatological Society and which is now in press to be reported in the *ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY*. This case is particularly interesting because it has the findings of both the Letterer-Siwe syndrome with lesions in the bone and cutaneous lesions at the same time, with a remarkable spontaneous recovery of the bone lesions and recovery of all the cutaneous lesions under irradiation.

This is a child of 16 months in whom at the age of 8 months there developed ulcerative and fungating lesions in the groin and on the tongue and on the buccal mucosa. The biopsies were initially performed. My associates and I had no suspicion of any bony lesions at this time. Under the microscope, the picture was one of a reticular structure with large numbers of histiocytes and eosinophils, and subsequent examination and reference of the slides to Dr. Hamilton Montgomery established a probable diagnosis of eosinophilic granuloma.

Then we had the roentgenologic demonstration of the bony lesions. These lesions were the ulcerative and fungating type of the skin. They were around the genitalia and in the axilla. There were lesions in the mouth and on the tongue and also a large lesion on the abdomen. I want to call attention here to the remarkable changes in the bones. There is a lesion which could readily be confused with a malignant growth, sarcoidosis and sporotrichosis.

Lesions in the skull and a second lesion scattered around the ribs are much like those of a malignant growth.

This was the microscopic picture, essentially—not altogether—the same as those shown by our president, but more like some of those shown by Dr Weidman but not very similar to those in Dr Lewis' case. There were large numbers of the eosinophilic cells throughout, and originally we felt that this was probably a reticuloendothelioma, for lack of a better diagnosis.

Under mild irradiation all the cutaneous lesions underwent complete resolution, and during the period of observation the lesion in the bone also completely disappeared, whether the latter disappeared under the influence of roentgen rays or whether they disappeared spontaneously is open to question. At no time were eosinophils found in the blood.

DR HAMILTON MONTGOMERY, Rochester, Minn. I was much interested in the excellent papers by Dr Weidman and by Dr Lewis and Dr Cormia.

Dr Burkhart and I wrote on tissue eosinophilia (*ARCH DERMAT & SYPH* 49 19-26 [Jan] 1944), but we missed the articles on eosinophilic granuloma of bone written by the general pathologists. Dr A C Broders called my attention to this condition some months ago, and I believe that there is no question that Dr Curtis' case to which Dr Wile referred in this discussion is one of that disease with cutaneous manifestations.

Dr Walter Lever is reporting a case of eosinophilic granuloma of the skin in which there were foam cells and which he suggests is related to eosinophilic granuloma of the bone. The latter condition belongs with Hand-Schuller-Christian disease. The general manifestations are not so severe as those of Letterer-Siwe disease. Farber, I believe, would withdraw these conditions from disorders of lipid metabolism, regarding any deposits of lipids as secondary and not primary factors. Yet, there are many cases of Hand-Schuller-Christian disease on record, including those reported by Dr Weidman and his associates with concomitant lesions of xanthoma disseminatum on the skin.

One of Dr Weidman's cases of eosinophilic granuloma of the skin, as he stated, was strongly suggestive of Hodgkin's disease. In Dr Lewis' case of eosinophilic granuloma, the question was raised of possible periarteritis nodosa. Whereas there was some thickening of the endothelium as shown in the slides that were projected, a typical one-sided involvement of all the muscle layers was not apparent. Rich, of Baltimore, has advocated an allergic basis for periarteritis nodosa. Eosinophilia of the blood or tissue, however, is not necessarily indicative of an allergic basis. Among other eosinophilic infiltrations of the skin one might include pemphigus vegetans, in which decided acanthosis together with microabscesses filled with eosinophils makes for a diagnostic picture.

DR CARROLL S WRIGHT, Philadelphia. I want to say a word about the treatment of the patient that Dr Weidman has mentioned. This woman came with a lesion that did not look unlike a chancre. She had been studied by two other dermatologists with that idea, who had advocated Wassermann tests, which elicited negative reactions, but no one had performed a biopsy. The lesion was about the size of a dime, so while I was taking a section for biopsy I thought that I would desiccate it. Healing was complete in two or three weeks.

She returned in March with an almost identical lesion, and, because of my experience with the other lesion, I again applied desiccation, with complete healing.

This would be applicable in small ulcerated lesions only, but I thought that it might be worth while to mention in case any dermatologists saw a similar case.

DR EARL W NETHERTON, Cleveland. After hearing these two excellent presentations, and particularly Dr Weidman's presentation, there seems to be con-

siderable doubt in my mind as to whether the case that I presented before the society last year as discoid lupus erythematosus with superimposed xanthomatous infiltration might not have been, in reality, an eosinophilic granuloma

A few weeks ago Dr Weidman corresponded with me, asking if we couldn't get this patient back. Since she lived out of the city, it was difficult to have her return. She did, however, return about two weeks ago, and the lesions on her face showed decided regression, leaving slight, thin, atrophic scarring. The xanthosis had decreased but had not completely disappeared. The erythematous phase of the eruption had almost entirely cleared up.

After hearing from Dr Weidman, I reviewed the sections again. Unfortunately, biopsy specimens were not obtained from the early portion of the lesion. However, I obtained two biopsy specimens, one in the strictly xanthomatous process and one taken where the lesion was erythematous but still showing the yellowish discoloration. In none of these sections were my associates and I able to find eosinophils. The eosinophilia at the present time is 5 per cent. She had a leukocyte count of 5,500.

I might state also that after my last observation she received bismarsen. How much this influenced the regression of the lesions, I am unable to state. However, I feel that my case may have been one of eosinophilic granuloma. However, we did not see the patient at a time when eosinophils could be demonstrated. This possibility will remain open to dispute until other similar cases have been observed.

Also, I should like to report briefly the case of a 3 month old child that had an eosinophilic granuloma of the groin with lesions involving the right scapula, the fifth rib and the eleventh dorsal vertebra. This child was born, so we are told by the family physician, with a papular eruption. The lesions when we saw the child were few, but they were uniformly pea sized and smooth, slightly scaly, dull red papules. The mother of the patient would not permit investigation at the time, stating that she would return later. She did return three weeks later, and the eruption had disappeared leaving varioliform scarring. The lesions in the bones at the present time are showing regression with irradiation.

Dr GEORGE M LEWIS, New York. Recently our patient had a rather severe exacerbation, and for want of something better to do, we gave him Benadryl, there was an immediate and striking response in the relief of itching. There was no change at all in the lesions themselves.

In spite of what Dr Montgomery said in his discussion, it would seem that the work of Rich and others has shown that periarteritis nodosa is not the invariably fatal disease that it was once considered, so that it may not be too far out of line to consider that some of these cases of eosinophilic granulomas border on the domain of that disease.

## EOSINOPHILIC GRANULOMA OF THE SKIN

Its Relation to Erythema Elevatum Diutinum and Eosinophilic Granuloma of the Bone, Report of a Case

WALTER F LEVER, M D

BOSTON

**T**HE CASE to be presented has many clinical and histologic features in common with erythema elevatum diutinum and with eosinophilic granuloma of the skin. Eosinophilic granuloma has been described as a disease of the skin and of the bone, but whether the two diseases are related is not yet certain.

In the following report the clinical and histologic appearance of erythema elevatum diutinum, eosinophilic granuloma of the skin and eosinophilic granuloma of the bone will be reviewed and the possibility of a relationship discussed.

### REPORT OF A CASE

A 47 year old woman first noticed in 1935 a small purple patch in the left malar region. In 1939 two additional lesions appeared, one on the right cheek and one just below the first lesion on the left cheek. All three patches gradually increased in size, and by 1942 the two on the left cheek had united. The lesions were not tender, and only when the patient was emotionally disturbed did the larger one on the left cheek swell slightly and throb. The patient stated that her general health had been good throughout these years.

Examination in 1945 revealed two purple lesions, one on each cheek (fig 1 A). The larger lesion on the left measured 5.5 by 5 cm, the smaller on the right, 2.3 by 2.8 cm. Both had sharply defined, irregular borders. The epidermis appeared normal except that the follicular openings were more prominent than is usual. The lesion on the left cheek (fig 1 B) presented diffuse infiltration at the upper and medial margins and irregular, nodular infiltration throughout. The infiltrate felt soft, almost elastic to the touch. The lesion on the right cheek was not infiltrated. The larger lesion showed, in areas in which the infiltration was more pronounced, an admixture of a yellowish brown hue. Aside from the cutaneous lesions, the physical examination revealed no abnormalities.

*Treatment*—The lesions were treated by roentgen rays between December 1941 and April 1943. A total of 2,200 r were administered to the small lesion on the right cheek and 1,600 r to the large lesion on the left. No effect was noted.

*Laboratory Data*—The results of urinalysis and several blood cell and differential counts were normal. The basal metabolic rate was —11 per cent. The serum cholesterol content measured 278 mg, nonprotein nitrogen 25 mg and protein 8.2 Gm per hundred cubic centimeters. Roentgenograms of the entire skeleton disclosed normal structure.

From the Departments of Dermatology and Pathology, Massachusetts General Hospital

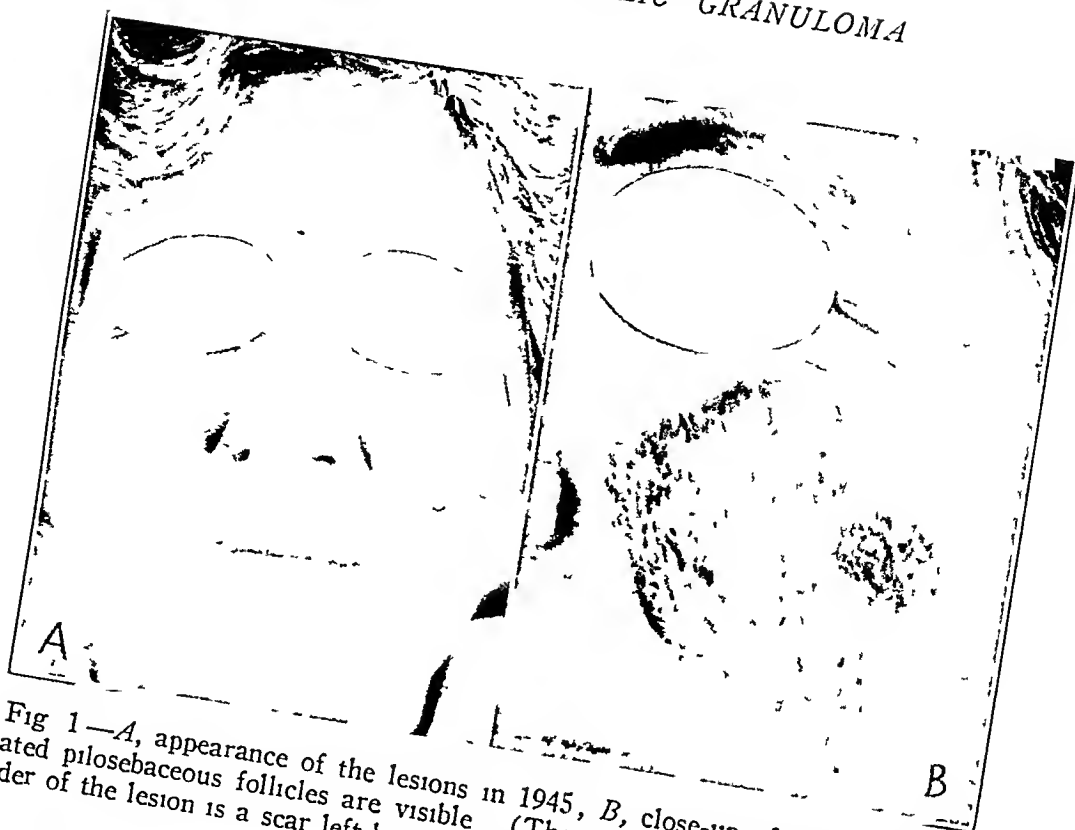


Fig 1—*A*, appearance of the lesions in 1945, *B*, close-up of the larger lesion. Dilated pilosebaceous follicles are visible. (The small white area near the lower border of the lesion is a scar left by taking a specimen for biopsy.)

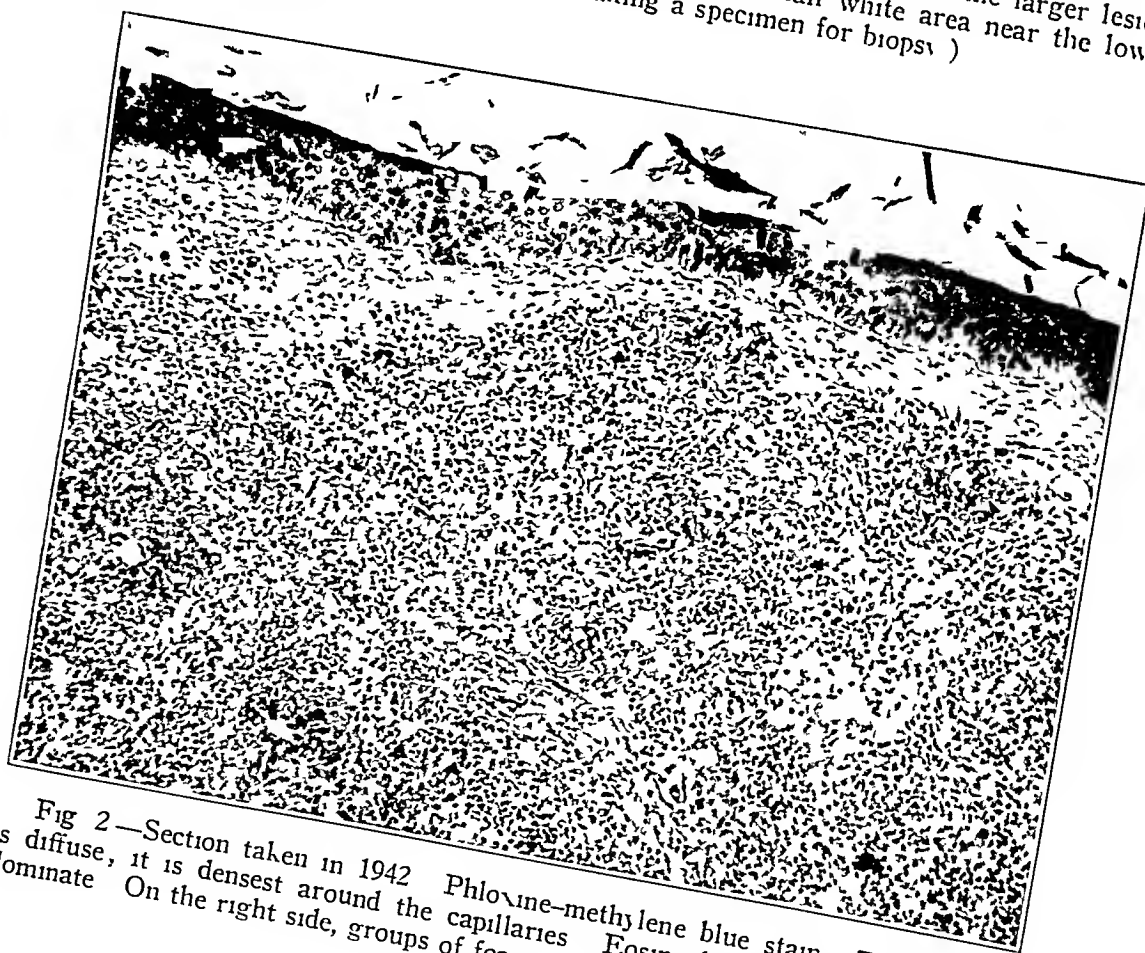


Fig 2—Section taken in 1942. Phloxine-methylene blue stain. The infiltrate is diffuse, it is densest around the capillaries. Eosinophils and neutrophils predominate. On the right side, groups of foam cells are present,  $\times 90$ .

*Bacteriologic Studies*—After a thorough cleansing of the skin with soap and alcohol, a piece of skin was removed, with the aid of a 6 mm biopsy punch, from an infiltrated area of the larger lesion. The specimen was divided into an upper portion, including the epidermis, and a lower portion. Aerobic and anaerobic

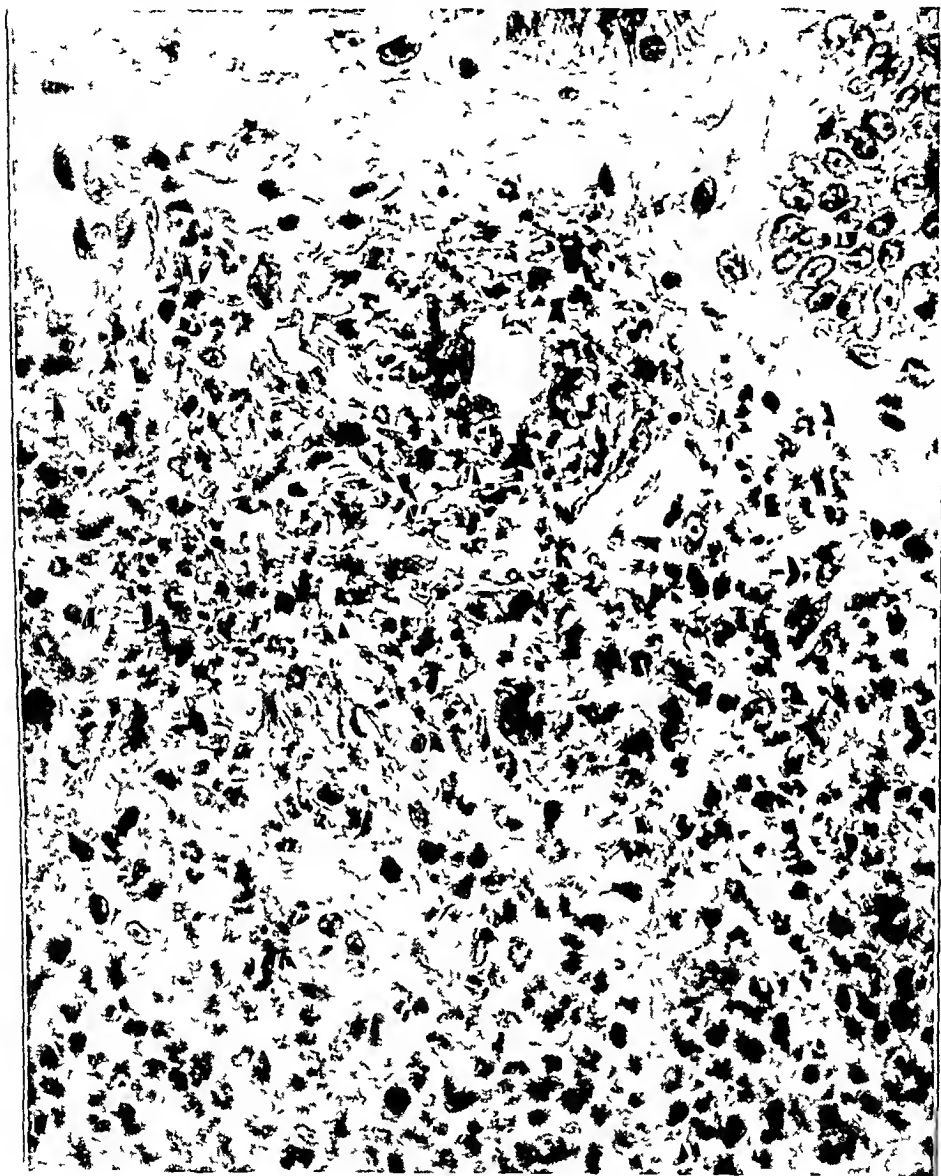


Fig 3—Section taken in 1942. Phloxine-methylene blue stain. A capillary surrounded by a dense infiltrate is shown. At the right lower quadrant of the capillary, swollen reticulum fibers are visible. (Normal reticulum fibers are not visible in phloxine-methylene blue stains),  $\times 375$

cultures resulted in no growth from the lower portion. Nonhemolytic streptococci grew in aerobic cultures from the upper portion. This growth was regarded as a contaminant, since saliva contains abundant nonhemolytic streptococci.

*Histologic Studies*—Four specimens for biopsy were obtained from the larger lesion on the left cheek, 1 in 1942 and 3 in 1945

The section obtained in 1942 showed an epidermis of normal thickness. The rete cones were nearly all flattened out. An extensive, extremely cellular infiltrate occupied the corium (fig 2). It was separated from the epidermis by a narrow rim of normal connective tissue. In the upper half of the corium the infiltrate was continuous, in the lower half it had essentially a perivascular arrangement. Here and there the infiltrate extended between the fat cells of the subcutaneous fat. The infiltrate was composed of many cell types: eosinophils, polymorphonuclear leukocytes, histiocytes (reticulum cells or monocytes), phagocytes, foam cells, fibroblasts, lymphocytes, plasma cells and mast cells. Although their proportionate number varied from place to place, eosinophils predominated everywhere. Most of them were polymorphonuclear, but some had a round nucleus. Neutrophils were fairly numerous, and in many instances it was impos-



Fig 4—Section taken in 1945. Aniline-methylene blue stain. The cellular infiltrate is patchy and separated by areas of fibrosis. Histiocytes and lymphocytes predominate. Numerous swollen reticulum fibers are visible. Foam cells are scattered throughout the field,  $\times 120$ .

sible to decide whether a cell was a neutrophil or an eosinophil. There were numerous histiocytes with large, pale, round or oval nuclei. Some of the histiocytes exhibited phagocytic properties, containing hemosiderin granules, fat vacuoles or both. A few large foam cells were present. In some areas the histiocytes showed development into fibroblasts. Lymphocytes and plasma cells were scattered in small numbers through the infiltrate. Mast cells were conspicuous because of their size and number. The blood vessels of the corium were dilated and their endothelium swollen. The cellular infiltrate was particularly dense in their vicinity. Phloxine-methylene blue stain (which does not stain normal reticulum fibers) showed swollen, intensely eosinophilic reticulum fibers around many of the blood vessels (fig 3). Thus the impression was gained that the vessels were

arterioles with greatly thickened and infiltrated walls. Elastic tissue stains, however, revealed no elastic fibers around the vessels and proved that the vessels were capillaries and precapillaries with perivascular infiltration.

The sections obtained in 1945 revealed slight hyperkeratosis with dilatation and keratotic plugging of some of the pilosebaceous follicles. The infiltrate was no longer continuous, but divided into irregular islands by areas of fibrosis (fig. 4).



Fig. 5—Section taken in 1945. Reticulum stain (Foot). There is a dense network of reticulum fibers. Many of them are swollen. On the right side and in the lower part of the field various stages of transformation of reticulum fibers into collagen fibers can be seen. Foam cells are present in the upper corium,  $\times 200$ .

In a few places the infiltrate was still composed predominantly of eosinophils and neutrophils, but in general it consisted mainly of histiocytes and lymphocytes. Many histiocytes contained vacuoles and hemosiderin granules. Foam cells were

conspicuous. At the periphery of the islands of infiltrate there were many fibroblasts laying down young connective tissue. Many swollen reticulum fibers were visible in phloxine-methylene blue and aniline blue (Mallory) stains. Reticulum stains stained after Foot (fig 5) showed a dense reticulum network within the cellular infiltrate, in many areas one could observe the gradual transformation of



Fig 6—Section taken in 1945. Phloxine-methylene blue stain. There is a considerable degree of fibrosis. Several vessels show thickening and fibrosis of their walls. The perivascular infiltrate of such vessels has been replaced by concentrically arranged collagen bundles,  $\times 250$ .

reticulum fibers into connective tissue fibers. The endothelial cells lining the blood vessels were large and increased in number. Some of the vessels located in areas of fibrosis had thick, fibrotic walls (fig 6). Polariscopic examination of stained

frozen sections revealed that the fat vacuoles within the phagocytes and the content of the foam cells were doubly refractile. This indicated that the fat contained cholesterol and cholesterol esters.

#### COMMENT

The clinical picture suggests the following diseases: sarcoid, xanthoma tuberosum, erythema elevatum diutinum and eosinophilic granuloma. On histologic grounds the first two can both be excluded, but erythema elevatum diutinum and eosinophilic granuloma deserve consideration.

Before discussing these two diseases, I wish to call attention to 2 cases recently reported by Anderson<sup>1</sup> and Netherton<sup>2</sup> which show a striking resemblance to the case reported in this paper and probably represent the same disease.

In Anderson's case, a woman aged 42 presented four lesions, one on each side of the neck and one on each cheek. They were sharply margined, slightly raised, plaquelike and erythematous with a distinct yellowish tinge. They had developed slowly in the course of nine years. The serum cholesterol content was normal. The following clinical diagnoses were considered: lupus erythematosus, xanthoma and sarcoid. A biopsy showed "xanthoma with definite fatty infiltration." No details of the histologic appearance were given.

In Netherton's case, a woman aged 45 presented on both cheeks, on the bridge of the nose and on the right ear—fairly well demarcated, raised, rounded and irregularly shaped plaques. The lesions had developed over a period of ten years. The more recent lesions were light red, the older lesions yellowish. The overlying epidermis was smooth, the pilosebaceous follicles were dilated. Histologic examination revealed an infiltrate composed of lymphocytes, fibroblasts, epithelioid cells and both large and small foam cells. The capillaries were dilated, and their endothelial cells were hyperplastic. In some areas the stroma was dense and fibrous, with less cellular infiltrate. A fat stain showed intracellular and extracellular deposits of doubly refractile lipids. Netherton thought that lupus erythematosus with superimposed xanthomatous infiltrate was the most likely diagnosis but pointed out that the histologic changes were not entirely consistent with lupus erythematosus. Weidman, in his discussion of Netherton's paper, raised the question whether this case, as well as all cases of extracellular cholesterosis, may not be erythema elevatum diutinum with superimposed extracellular cholesterosis.

1 Anderson, N. P. (a) A Case for Diagnosis (Xanthoma?), *Arch. Dermat. & Syph.* **48**: 471 (Oct.) 1943, (b) Systemic Xanthoma, *ibid.* **49**: 149 (Feb.) 1944.

2 Netherton, E. W. Chronic Discoid Lupus Erythematosus With Superimposed Xanthomatous Infiltration, *Arch. Dermat. & Syph.* **51**: 100 (Feb.) 1945.

The histologic picture of Netherton's case greatly resembles that presented by the later sections of the case reported herein. The only difference lies in the presence of eosinophils and neutrophils in my case. Since their number was much smaller in the later than in the earlier sections, it is conceivable that future sections, if taken, may not show any of these cells, so that the resemblance to Netherton's case would then be complete.

*1 Erythema Elevatum Diutinum* This is a rare dermatosis. In a review of the literature only 20 cases were found to which this diagnosis could be applied without reservation. Of these, 14 belonged to the "Hutchinson type"<sup>3</sup> and 6 to the "Bury type"<sup>4</sup>. The early lesions of erythema elevatum diutinum are papules and nodules which may, by peripheral extension and by confluence with neighboring lesions, increase into large plaques. Their color is red or purplish, their consistency soft to moderately firm. The most commonly involved sites are the extensor surfaces of the extremities, particularly the areas overlying the joints. Next commonly, the face, ears and buttocks are affected. In most cases the number of lesions is considerable, in 2 cases, however,

3 (a) Hutchinson, J. On Two Remarkable Cases of Symmetrical Purple Congestion of the Skin in Patches, with Induration, *Brit J Dermat* 1:10, 1888-1889, (b) Two Additional Cases of Purple Patches on the Skin. History of Gout in Both, *Arch Surg* 1:372, 1889-1890. (c) Audry, C. Des érythémato-scléroses et, particulièrement, de l'érythémato-sclérose pemphigoïde, *Ann de dermat et syph* 5 1, 1904. (d) Dalla Favera, G. B. Beitrag zum Studium des sogenannten Granuloma annulare (R. Crocker), éruption circinée chronique de la main (Dubreuilh), *Dermat Ztschr* 16 73, 1909, (e) Erythema elevatum diutinum und Granuloma annulare, *ibid* 18:541, 1910. (f) Piccardi, G. Erythema elevatum et diutinum, *Dermat Wchnschr* 55:1115, 1912. (g) Frühwald, R. Fall von Erythema elevatum, *ibid* 63:995, 1916. (h) Weidman, F. D. Xanthoma en tumeurs, *Arch Dermat & Syph* 11:566 (April) 1925, (i) Erythema Elevatum Diutinum, *ibid* 14 622 (Nov.) 1926. (j) Weidman, F. D., and Besançon, J. H. Erythema Elevatum Diutinum. Rôle of Streptococci, and Relationship to Other Rheumatic Dermatoses, *ibid* 20 593 (Nov.) 1929. (k) Combes, F. C., and Bluefarb, S. M. Erythema Elevatum Diutinum, *ibid* 42 441 (Sept.) 1940. (l) Engman, M. F., Jr., Pfaff, R. O., and Cooper, Z. K. Erythema Elevatum Diutinum, *ibid* 45 334 (Feb.) 1942. (m) Ketron, L. W. Erythema Elevatum Diutinum, *ibid* 50:363 (Dec.) 1944.

4 (a) Bury, J. S. A Case of Erythema with Remarkable Nodular Thickening and Induration of Skin, Associated with Intermittent Albuminuria, *Illust M News* 3:145, 1889. (b) Hutchinson, J. Peculiar Disease of Skin of Hands (Bury's Case), *Arch Surg* 2 301, 1890-1891 [plate 61], (c) Crocker, H. R., and Williams, C. Erythema Elevatum Diutinum, *Brit J Dermat* 6 1 and 33, 1894. (d) Smith, F. J. A Case of So-Called Erythema Elevatum Diutinum, *ibid* 11.144, 1894. (e) Zweig, L. Ueber einen Fall von Erythema elevatum et diutinum, *Arch f Dermat. u Syph* 109 519, 1911. (f) Trimble, W. B. Erythema Elevatum Diutinum. Report of a Case, with Comments on Its Nosologic Positions, *Arch Dermat & Syph* 13 383 (March) 1926. (g) Gray, A. M. H. Erythema Elevatum Diutinum, *Proc Roy Soc Med* 25 1743, 1932.

(Trimble's case <sup>4f</sup> and Hutchinson's fourth case <sup>3b</sup>) there were only two plaques, and in 2 others, (Gray's case <sup>4e</sup> and Hutchinson's third case <sup>3b</sup>) a single plaque. In Hutchinson's fourth case the two plaques were located on the forehead. The evolution of the lesions may follow several courses: they may persist as soft plaques (Hutchinson type), they may develop into hard, fibrotic, keloid-like plaques (Bury type), or they may undergo involution. The color of the soft plaques may remain purple or change to a yellowish brown. The yellowish tint is, according to Weidman,<sup>5</sup> caused by hemoglobin or hematin. The duration of erythema elevatum diutinum may be from one to many years. In Piccardi's case <sup>3f</sup> the disease lasted fourteen months, in Dalla Favera's second case <sup>3e</sup> two and a half years. In all other cases the disease was still active at the time of reporting. In 5 cases <sup>6</sup> the disease had already persisted for five years or longer.

Histologic examination was carried out in 15 cases, that is, in all except those reported by Hutchinson <sup>3a, b</sup> and Bury <sup>4a, b</sup>. For practical purposes the histologic picture may be divided into three stages. In the first stage (Hutchinson type) the microscopic picture is dominated by a dense infiltrate in which polymorphonuclear leukocytes predominate. They show no tendency to disintegrate. In addition to the polymorphonuclear leukocytes, lymphocytes, plasma cells, histiocytes, fibroblasts and, occasionally, epithelioid cells <sup>3k, l</sup> and mast cells <sup>7</sup> are present. In 3 cases <sup>8</sup> a few eosinophils, and in 1 case <sup>3k</sup> numerous eosinophils were observed. The capillaries usually are dilated and their endothelium swollen. The perivascular reticulum fibers may show hyaline degeneration <sup>9</sup>. In the second stage, the cellular infiltrate has decreased in density and has essentially a perivascular arrangement. Polymorphonuclear leukocytes and lymphocytes are fewer, and fibroblasts predominate. There is beginning fibrosis separating the cellular infiltrate into irregularly shaped islands. In the third stage (Bury type) fibrosis dominates the picture. The cellular infiltrate is greatly reduced, and polymorphonuclear leukocytes are entirely absent. Frequently, the walls of the capillaries also show fibrosis. Evidence of phagocytosis was present in 4 cases. Dalla Favera <sup>3d, e</sup> described in his 2 cases the presence of phagocytes containing erythrocytes and nuclear debris, Engman <sup>3l</sup> observed hemosiderin within phagocytes, Trimble <sup>4f</sup> noticed foci of large cells with foamy cytoplasm.

5 Weidman, F. D. The Pathology of the Yellowing Dermatoses, *Arch Dermat & Syph* **24** 954 (Dec.) 1931.

6 Hutchinson <sup>3a</sup> Weidman <sup>3h, i</sup> Weidman and Besançon <sup>3j</sup> Engman <sup>3l</sup> Ketron <sup>3m</sup> Trimble <sup>4f</sup>.

7 Audry <sup>3c</sup> Dalla Favera <sup>3d, e</sup> Piccardi <sup>3f</sup>.

8 Dalla Favera <sup>3d</sup> Weidman <sup>3h, i</sup> Weidman and Besançon <sup>3j</sup> Ketron <sup>3m</sup>.

9 Dalla Favera <sup>3e</sup> Weidman <sup>3h, i</sup> Weidman and Besançon <sup>3j</sup> Combes <sup>3i</sup> Engman <sup>3l</sup> Ketron <sup>3m</sup>.

*2 Eosinophilic Granuloma* Eosinophilic granuloma has been described in two organs, the bone and the skin. In no case were osseous and cutaneous lesions present simultaneously. Whether eosinophilic granuloma of the bone and of the skin represent the same disease has so far not been discussed in the literature.

(a) *Eosinophilic Granuloma of the Bone* This is a benign, destructive lesion affecting one, several or many bones. The first instance was recorded in the literature by Finzi<sup>10</sup> in 1929, but only in 1940 did Otani and Ehrlich<sup>11</sup> and Lichtenstein and Jaffe<sup>12</sup> establish eosinophilic granuloma of the bone as a well defined disease entity. Up to the present a total of 44 cases have been described.<sup>13</sup> Locally there may be swelling, tenderness and pain, but some lesions are asymptomatic. With the possible exception of the bones of the hands and feet, any bone may be the site of lesions. Mainly the cranial vault, the ribs, the vertebrae, the humeri and the femurs are involved. The

10 Finzi, O. Mieloma con prevalenza della cellule eosinofile, circoscritto all'osso frontale in un giovane di 15 anni, *Minerva med* **9** 239, 1929.

11 Otani, S., and Ehrlich, J. C. Solitary Granuloma of Bone Simulating Primary Neoplasm, *Am J Path* **16** 479, 1940.

12 Lichtenstein, L., and Jaffe, H. L. Eosinophilic Granuloma of Bone, with Report of a Case, *Am J Path* **16** 595, 1940.

13 (a) Mignon, F. Ein Granulationstumor des Stirnbeins, *Fortschr a d Geb d Rontgenstrahlen* **42** 749, 1930. (b) Schairer, E. Ueber eine eigenartige Erkrankung des kindlichen Schadels (Osteomyelitis mit eosinophiler Reaktion), *Zentralbl f allg Path u path Anat* **71** 113, 1938. (c) Eosinophilic Granuloma of Bone, Cabot Case 26302, *New England J Med* **223** 149, 1940. (d) Hatcher, C. H. Eosinophilic Granuloma of Bone, *Arch Path* **30**:828 (Sept) 1940. (e) Farber, S. The Nature of "Solitary or Eosinophilic Granuloma" of Bone, *Am J Path* **17** 625, 1941. (f) Green, W. T., and Farber, S. "Eosinophilic or Solitary Granuloma" of Bone, *J Bone & Joint Surg* **24** 499, 1942. (g) Bass, M. H. Solitary Eosinophilic Granuloma of Bone, *Am J Dis Child* **61** 1254 (June) 1941. (h) Gross, P., and Jacob, H. W. Eosinophilic Granuloma and Certain Other Reticuloendothelial Hyperplasias of Bone, *Am J M Sc* **203** 673, 1942. (i) Thoma, K. Eosinophilic Granuloma with Report of One Case Involving First the Mandible, Later Other Bones, and Being Accompanied by Diabetes Insipidus, *Am J Orthodontics (Oral Surg Sect)* **29** 641, 1943. (j) Jaffe, H. L., and Lichtenstein, L. Eosinophilic Granuloma of Bone. A Condition Affecting One, Several or Many Bones, but Apparently Limited to the Skeleton, and Representing the Mildest Clinical Expression of the Peculiar Inflammatory Histiocytosis Also Underlying Letterer-Siwe Disease and Schuller-Christian Disease, *Arch Path* **37** 99 (Feb) 1944. (k) Mallory, T. B. Medical Progress. Pathology, Diseases of the Bone, *New England J Med* **227** 955, 1942. (l) Schairer, E. Osteomyelitis mit eosinophiler Reaktion (Eosinophiles Granulom des Knochens), *Deutsche Ztschr f Chir* **258**:637, 1944. (m) Engelbreth-Holm, J., Teilmann, G., and Christensen, E. Eosinophil Granuloma of Bone—Schuller-Christian's Disease, *Acta med Scandinav* **118** 292, 1944. (n) Solomon, H. A., and Schwartz, S. Eosinophilic Granuloma of Bone, *J A M A* **128** 729 (July 7) 1945. Finzi<sup>10</sup> Otani and Ehrlich<sup>11</sup> Lichtenstein and Jaffe<sup>12</sup>

lesions were single in 31 and multiple in 13 of the 44 cases described. The lesions tend to heal spontaneously in the course of several months or years and are radiosensitive.

Histologic examination in the early stage reveals a granulomatous process in which two types of cells, eosinophils and histiocytes (reticulum cells), predominate. The eosinophils usually are polymorphonuclear, but occasionally<sup>14</sup> mononuclear eosinophils are also present. Finzi,<sup>10</sup> Farber<sup>13e,f</sup> and Thoma<sup>13i</sup> regarded them as eosinophilic myelocytes. Jaffe and Lichtenstein,<sup>13j</sup> however, stated that they were too small to be regarded as such. The histiocytes are actively phagocytic and may contain cellular debris,<sup>15</sup> finely divided lipid<sup>16</sup> or hemosiderin.<sup>17</sup> The lipid as a rule is isotropic, but occasionally it is anisotropic.<sup>18</sup> There are, in addition, variable numbers of plasma cells, lymphocytes and polymorphonuclear leukocytes. Not infrequently phagocytic multinuclear giant cells are found.<sup>19</sup> There may be foci of necrosis and hemorrhage.<sup>20</sup> Numerous capillaries are present. The endothelial cells of the capillary walls may be swollen.<sup>13h</sup> Jaffe and Lichtenstein observed multiplication of the adventitial cells and their transformation into histiocytes.

At a later stage the number of eosinophils is greatly reduced, they may even be entirely absent.<sup>13e,f</sup> Histiocytes are then the most commonly found type. They frequently are vacuolated and may assume the appearance of foam cells.<sup>21</sup> The fat which they contain usually is isotropic, but may be anisotropic.<sup>22</sup> In addition, there is ingrowth of fibroblasts. Fibroblasts increase in number as the lesion ages, and

14 Finzi<sup>10</sup> Farber<sup>13e</sup> Green and Farber<sup>13f</sup> Thoma<sup>13i</sup> Jaffe and Lichtenstein<sup>13j</sup>

15 Finzi<sup>10</sup> Lichtenstein<sup>12</sup> Hatcher<sup>13d</sup> Farber<sup>13e</sup> Green and Farber<sup>13f</sup> Jaffe and Lichtenstein<sup>13j</sup>

16 Otani and Ehrlich<sup>11</sup> Schairer<sup>13b</sup> Farber<sup>13e</sup> Green and Farber<sup>13f</sup> Bass<sup>13g</sup> Gross and Jacob<sup>13h</sup> Thoma<sup>13i</sup> Jaffe and Lichtenstein<sup>13j</sup> Engelbreth-Holm, Teilum and Christensen<sup>13m</sup>

17 Otani and Ehrlich<sup>11</sup> Lichtenstein and Jaffe<sup>12</sup> Schairer<sup>13b,1</sup> Farber<sup>13e</sup> Green and Farber<sup>13f</sup> Jaffe and Lichtenstein<sup>13j</sup>

18 Farber<sup>13e</sup> Green and Farber<sup>13f</sup> Jaffe and Lichtenstein<sup>13j</sup> Engelbreth-Holm, Teilum and Christensen<sup>13m</sup>

19 Finzi<sup>10</sup> Otani and Ehrlich<sup>11</sup> Schairer<sup>13b,1</sup> Footnote 13c Farber<sup>13e</sup> Green and Farber<sup>13f</sup> Bass<sup>13g</sup> Gross and Jacob<sup>13h</sup> Thoma<sup>13i</sup> Engelbreth-Holm, Teilum and Christensen<sup>13m</sup>

20 Otani and Ehrlich<sup>11</sup> Hatcher<sup>13d</sup> Farber<sup>13e</sup> Green and Farber<sup>13f</sup> Bass<sup>13g</sup> Jaffe and Lichtenstein<sup>13j</sup> Schairer<sup>13i</sup> Solomon and Schwartz<sup>13n</sup>

21 Otani and Ehrlich<sup>11</sup> Farber<sup>13e</sup> Green and Farber<sup>13f</sup> Jaffe and Lichtenstein<sup>13j</sup> Gross and Jacob<sup>13h</sup> Engelbreth-Holm, Teilum and Christensen<sup>13m</sup>

22 Farber<sup>13e</sup> Green and Farber<sup>13f</sup> Engelbreth-Holm, Teilum and Christensen<sup>13m</sup>

gradually the granulomatous process is replaced by connective tissue<sup>23</sup> Jaffe and Lichtenstein presented evidence that eosinophilic granuloma may heal through resolution instead of through the intermediary steps of lipidization and connective-tissue scarring

Farber<sup>13e,f</sup> first recognized the pathogenesis of eosinophilic granuloma correctly He concluded that eosinophilic granuloma, Hand-Schuller-Christian disease and Letterer-Siwe disease represented "variations in degree, stage of development and localization of the same basic disease process" With one exception,<sup>13l</sup> all authors<sup>24</sup> who have since written on eosinophilic granuloma of the bone have accepted this point of view These three diseases are now regarded as histiocytoses (reticulo-endothelioses) The concept of Hand-Schuller-Christian disease as a primary disturbance of the lipid metabolism (xanthomatosis) has been abandoned<sup>13k</sup> and the presence of cholesterol is regarded as a secondary infiltration If the histiocytosis occurs in infancy it is generalized and rapidly fatal (Letterer-Siwe disease), and the time required for development of the lesion into a lipogranuloma is not available In early childhood the disease is chronic (Hand-Schuller-Christian disease) and lipidization usually is pronounced, with few or no eosinophils In later childhood or in adulthood the usual picture is that of eosinophilic granuloma Transitional cases between these three forms of histiocytosis are on record<sup>25</sup>

Letterer-Siwe disease and Hand-Schuller-Christian disease affect the skin, in addition to the bones and other organs, in about a third of the cases<sup>26</sup> On the other hand, cutaneous lesions have never been described in conjunction with eosinophilic granuloma of the bone

(b) Eosinophilic Granuloma of the Skin The first cases (later classified as eosinophilic granuloma of the skin by the author himself) were described by Martinotti<sup>27</sup> in 1923 Nanta and Gadrat<sup>28</sup> established the term eosinophilic granuloma of the skin in 1937 Eleven cases in

23 Otani and Ehrlich<sup>11</sup> Farber<sup>13e</sup> Green and Farber<sup>13f</sup> Gross and Jacox<sup>13h</sup>

24 Bass<sup>13g</sup> Gross and Jacox<sup>13h</sup> Thoma<sup>13i</sup> Jaffe and Lichtenstein<sup>13j</sup> Mallory<sup>13k</sup> Engelbreth-Holm, Teilum and Christensen<sup>13m</sup> Solomon and Schwartz<sup>13n</sup>

25 Farber<sup>13e</sup> Green and Farber<sup>13f</sup> Gross and Jacox<sup>13h</sup> Engelbreth-Holm, Teilum and Christensen<sup>13m</sup>

26 Lane, C W, and Smith, M G Cutaneous Manifestations of Chronic (Idiopathic) Lipoidosis (Hand-Schuller-Christian Disease), Arch Dermat & Syph **39** 617 (April) 1939

27 Martinotti, L (a) Contributo allo studio della eosinofilia istigena cutanea, Arch per le sc med **46** 259, 1923, (b) Zur Frage des eosinophilen Granuloms, Dermat Wchnschr **112** 25, 1941

28 Nanta, A, and Gadrat, J Sur un granulome éosinophilique cutané, Bull Soc franç de dermat et syph **44**:1470, 1937

all have been recorded with this diagnosis.<sup>29</sup> Whereas the cases described as eosinophilic granuloma of the bone represent a well established entity both clinically and histologically, those described as eosinophilic granuloma of the skin show uniformity only in their histologic, but not in their clinical, appearance. Probably not all cases described as eosinophilic granuloma should be regarded as such. On the basis of the clinical data supplied, it appears advisable to exclude Martinotti's 3 cases<sup>27</sup> and Lapiere's case<sup>29c</sup>. Martinotti's case 1 probably represented a pyogenic ulcer, his case 2 a systemic moniliasis and his case 3 an allergic eruption. Lapiere's case was one of malignant lymphoma (Hodgkin's disease). Of the remaining 7 cases, 5<sup>30</sup> were clinically characterized by nodular and plaque-like lesions of chronic course. In 2 cases<sup>31</sup> the lesions were vegetating. The latter 2 cases appeared sufficiently different from the other 5 cases to make one suspect that they represented a different disease.

Because of the complexity of the clinical picture in most of the reported cases, it is impossible to delineate each case adequately in a limited space. The reader is referred to the reviews recently published by Martinotti<sup>27b</sup> and Cerutti<sup>29e</sup>. However, since the literature on eosinophilic granuloma of the skin has never been reviewed in the English language literature, a short abstract of each reported case will be given.

Martinotti's first patient<sup>27</sup> was a young soldier who for several months had had on one leg an ulcer the size of a large coin and surrounded by an area of infiltration of doughy consistency. Excision of the ulcer was followed by recovery.

Martinotti's second patient<sup>27</sup> had a diffuse cutaneous eruption composed of papules, nodules, vesicles and pustules. The patient recovered after many months. *Cryptococcus ruber* Demme was obtained from the cutaneous lesions, the blood and the urine on several occasions.

29 (a) Freund, E. Su un caso di strani tumori cutanei in una tubercolosa, *Dermosifilograf* 5 617, 1930. (b) Pautrier, L. M., Glasser, R., and Labourgade, A. Lesions verruqueuses, vegetantes, elephantiasiformes, du pourtour de l'orifice anal, de tout le pli fessier et du scrotum, s'accompagnant de lesions vegetantes endorectales pouvant faire penser a une maladie de Nicolas-Favre, mais de nature indeterminee, *Bull Soc franç de dermat et syph* 43 896, 1936. (c) Lapiere, S. Un cas de granulome eosinophilique, *Bull Soc franç de dermat et syph* 44 1479, 1937. (d) Pasini, A. Granuloma eosinofilo (reticulo-endoteliosi proliferativa), *Gior ital di dermat e sif* 81 1, 1940. (e) Cerutti, P. Il granuloma eosinofilo, *Dermatologica* 85 90, 1942. (f) Lewis, G. M. A Case for Diagnosis (*Erythema Nodosum*?) *Arch Dermat & Syph* 48 436 (Oct) 1943. (g) Eosinophilic Granuloma, *ibid* 51 144 (Feb) 1945. (h) Wigley, J. E. M. ?Sarcoid of Boeck, ?Eosinophilic Granuloma, *Brit J Dermat* 57 68, 1945. Martinotti<sup>27a, b</sup> Nanta and Gadrat<sup>28</sup>

30 Freund<sup>29a</sup> Pasini<sup>29d</sup> Cerutti<sup>29e</sup> Lewis<sup>29f</sup> & Wigley<sup>29h</sup>

31 Nanta and Gadrat<sup>28</sup> Pautrier, Glasser and Labourgade<sup>29b</sup>

In Maitinotti's third patient<sup>27</sup> the illness lasted only fifteen days. Large umbilicated bullae on infiltrated red bases were present on the dorsa of both hands.

Freund's patient<sup>29a</sup> showed livid red, hard, painless nodes of six years' duration on face, shoulders and extremities. Roentgen ray therapy resulted in the patient's recovery.

Pautrier, Glasser and Labourgade<sup>29b</sup> reported the case of a patient with extensive perianal and endorectal vegetating lesions of six months' duration.

Nanta and Gadrat's patient<sup>28</sup> had perianal and endorectal vegetating lesions similar to those of the preceding patient and, in addition, vegetating tumefactions of the gums. The lesions were still progressing when the patient was last seen, nearly two years after the onset of the disease.

In Lapière's patient<sup>29c</sup> the disease began with an erythematous, bullous, papular and nodular eruption of generalized distribution. These lesions continued to appear for years but were then gradually superseded by hypertrophic sclerotic lesions. Sixteen years after the onset of the disease numerous large, hard lymph nodes were first felt. Soon afterward, the patient died of his disease.

Cerutti<sup>29e</sup> observed a patient in whom numerous nodular lesions of generalized distribution had been present for three months. In the more severely involved areas the nodules had coalesced into large plaques. In the genitocrural folds the lesions resembled syphilitic condylomas. Roentgen ray therapy caused the rapid disappearance of all the lesions. Soon afterward, however, the patient died, of lymphosarcoma of the cervical lymph nodes.

In Lewis' patient,<sup>29f,g</sup> crops of erythematous nodes and plaques had been appearing and disappearing for more than three years. They cleared without scarring. The majority of the lesions were located on the lower extremities.

The following 2 cases closely resemble the case reported in this paper.

Pasini's patient<sup>29d</sup> first noticed an indurated plaque on the right side of her forehead eight years before her admission to the hospital for treatment. This slowly increased in size until, finally, it covered all of the right half of the forehead and part of the left half. Three years before admission two other plaques had appeared, symmetrically placed before and below each ear. Two years before admission a fourth plaque had appeared in the submental region. The lesions presented a rounded, elevated border and a convex tumefaction covered by normal epidermis. They had a nearly homogeneous red cyanotic color and were of hard elastic consistency. Roentgen ray therapy resulted in the almost complete clearing of the lesions.

Wigley's patient<sup>29h</sup> presented on her forehead and nose four lesions which had appeared during the two years preceding her admission. They were smooth, grayish brown, slightly raised and infiltrated. They varied in size up to 1 cm.

Histologic examination revealed a similar picture in all but Lapiere's case<sup>29c</sup>. This case presented, in addition to the large number of eosinophils, numerous atypical reticulum cells and, in Lapiere's own opinion, was one of "malignant reticulo-endotheliosis". The histologic appearances of the remaining 10 cases may be discussed together. They showed a dense polymorphous infiltrate of the corium. In some cases<sup>32</sup> this infiltrate extended into the subcutaneous fat. In others it had led to erosion of the epidermis and to ulceration. Eosinophils and histiocytes predominated. Martinotti,<sup>27</sup> Pasini<sup>29d</sup> and Cerutti<sup>29e</sup> observed not only polymorphonuclear but also mononuclear eosinophils and histiocytes with eosinophilic granules. They observed intermediary stages between these forms of eosinophils and regarded the eosinophils as of histiogenic rather than of myeloid origin. In addition, polymorphonuclear leukocytes, lymphocytes, plasma cells and fibroblasts were present in varying amounts. In 5 cases<sup>32</sup> mast cells, and in 3 cases<sup>33</sup> epithelioid cells were present. Giant cells, resembling either megakaryocytes or Langhans' cells, were observed in 1 case<sup>29a</sup>. The infiltrate was well vascularized and, frequently, the endothelial cells and the walls of the vessels showed proliferation<sup>34</sup>. The evolution of eosinophilic granuloma is as yet little known. Only one author, Pautrier,<sup>29b</sup> reported the histologic appearance of an early and of a late lesion. In the late lesion the eosinophils had almost entirely disappeared, the infiltrate was more monomorphic, consisting mainly of plasma cells and lymphocytes, and was divided into islands by the ingrowth of collagen. Beginning fibrosis was noted also by Freund<sup>29a</sup> and Pasini<sup>29d</sup>.

3 *Relation of Eosinophilic Granuloma of the Skin to Eosinophilic Granuloma of the Bone and to Erythema Elevatum Diuturnum*—(a) Eosinophilic Granuloma of the Skin and of the Bone. Only one writer, Freudenthal,<sup>35</sup> has so far drawn attention to the fact that in the medical literature two diseases have been described under the name of eosinophilic granuloma, one as occurring in the skin and the other as occurring in the bones. He has assumed that they are identical, but has given no reasons for his belief.

In favor of their being the same disease is the great similarity of their histologic appearance. However, this is in no way specific since many types of granulation tissue contain eosinophils and histiocytes.

32 Martinotti<sup>27a b</sup> Freund<sup>29a</sup> Pasini<sup>29d</sup>

33 Martinotti<sup>27a b</sup> Freund<sup>29a</sup> Cerutti<sup>29e</sup>

34 Martinotti<sup>27a b</sup> Freund<sup>29a</sup> Pasini<sup>29d</sup> Cerutti<sup>29e</sup>

35 Freudenthal W, in discussion on Wigley<sup>29h</sup>



cases<sup>37</sup> In addition to leukocytes and histiocytes, there are found lymphocytes, fibroblasts and, occasionally, plasma cells and mast cells in the histologic picture of both diseases The vascular walls may be invaded by the cellular infiltrate and show evidence of degeneration, both in erythema elevatum diutinum<sup>9</sup> and in eosinophilic granuloma<sup>38</sup> In both diseases the infiltrate may persist essentially unchanged, may resolve or may gradually be replaced by fibrous tissue

Thus, it appears that there is sufficient similarity in the clinical and the histologic appearance of both eosinophilic granuloma of the skin and erythema elevatum diutinum to permit speculation as to a possible relationship

#### NOSOLOGIC POSITION OF THE REPORTED CASE

In its clinical appearance the case reported could pass as an instance of the early stage of erythema elevatum diutinum Although numerous lesions are the rule in erythema elevatum diutinum, in 4 cases from the literature there were only one or two lesions The presence of soft, purplish partly yellowish plaques, the absence of subjective symptoms and the chronicity of the lesion are consistent with a diagnosis of erythema elevatum diutinum Histologically, the presence of neutrophils and the degeneration of the perivascular reticulum fibers in the first biopsy and the beginning fibrosis in the later biopsies are compatible with a diagnosis of erythema elevatum diutinum Yet, the two most striking features of the case were the presence of a great number of eosinophils and foam cells These are uncommon features for erythema elevatum diutinum, since eosinophils were observed in only 4 cases and foam cells in only 1 case

Compared with eosinophilic granuloma of the skin, the case reported bears, in its clinical appearance, great resemblance to the cases described by Pasini<sup>29d</sup> and Wigley,<sup>29b</sup> in which there were plaque-like lesions limited to the face In contrast to Pasini's case roentgen ray therapy did not cause improvement of the lesions In its histologic appearance, the case resembles eosinophilic granuloma of the skin, so far as it showed a dense polymorphous infiltrate in which eosinophils predominated The vascular changes seen have been noted also in some cases of eosinophilic granuloma of the skin The only major difference consists in the pronounced phagocytic activity of the histiocytes and the presence of foam cells in the case reported

In contrast to eosinophilic granuloma of the skin, phagocytic activity is conspicuous in eosinophilic granuloma of the bone, resulting in the accumulation of hemosiderin and fat in the histiocytes and the formation of foam cells It can thus be stated that the histologic picture,

37 Dalla Favera,<sup>3d</sup> Engmann, Pfaff and Cooper,<sup>3b</sup> Trimble<sup>4f</sup>

38 Martinotti,<sup>27a,b</sup> Freund<sup>29a</sup>

with its predominance of eosinophils and foam cells, resembles that of eosinophilic granuloma of the bone more than that of either eosinophilic granuloma of the skin or erythema elevatum diutinum. If one would accept the diagnosis of eosinophilic granuloma in the case presented, it would provide an argument in favor of the identity of eosinophilic granuloma of the skin and of the bone.

In conclusion, the diagnosis in the case reported must remain open. It is suggested that the case is one of eosinophilic granuloma of the skin, a disease which may be related both to eosinophilic granuloma of the bone and to erythema elevatum diutinum.

#### SUMMARY

A woman has had for ten years three gradually enlarging soft plaques on her cheeks. Histologic examination in 1942 revealed an extremely cellular, granulomatous infiltrate in which eosinophils and histiocytes predominated. A few foam cells were also present. Histologic sections obtained three years later revealed a considerable decrease in the number of eosinophils but an increase in the number of foam cells and a beginning fibrosis.

No description of any dermatosis with this histologic picture was encountered in the literature. The histologic appearance was identical with that of eosinophilic granuloma of the bone. In many aspects it resembled that of eosinophilic granuloma of the skin and of erythema elevatum diutinum.

A diagnosis of eosinophilic granuloma of the skin is suggested.

It is possible that eosinophilic granuloma of the skin, eosinophilic granuloma of the bone and erythema elevatum diutinum are related diseases. These three diseases have in common, in the early stage, a granulomatous, extremely cellular infiltrate in which neutrophils or eosinophils predominate. This infiltrate may persist, may resolve or undergo fibrosis. In the fibrotic stage neutrophils and eosinophils are few and may be entirely absent. Phagocytic cells containing lipid and hemosiderin, and foam cells may or may not be present.

# GRANULOMATOUS HODGKIN'S DISEASE OF THE SKIN WITH EXTREME EOSINOPHILIA

(Eosinophilic Granuloma of the Skin?)

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COMMONLY, Hodgkin's disease expresses itself on the skin in a nonspecific manner, such as by pruritus, urticaria and scaly erythrodermas. Relatively seldom do granulomatous lesions appear. In our case, five biopsies of specimens of the skin and two of specimens of the lymph nodes furnished an unusual opportunity for correlation of the reactions in these two tissues and for observation of the tissue processes from their beginning to maturity. Moreover, polymorphonuclear leukocytes were present in enormous numbers, the neutrophilic ones, which are so rare in this disease, bespoke an acute type of reaction, and the eosinophilic ones raised the question of whether eosinophilic granuloma of the skin was related.

## REPORT OF A CASE

The patient was first seen at Grady Hospital on May 29, 1935, with a complaint of painful menstruation. The past history was essentially noncontributory and insignificant. The blood pressure was 160 systolic and 95 diastolic. The other physical findings were essentially normal. The patient was not seen again until June 26, 1941, when she returned with a complaint of pains in her arms and shoulders and also of "food souring" in her stomach. She complained of gastric distress after eating potatoes and beans. The physical examination revealed no significant findings, and she improved under symptomatic treatment.

On May 26, 1943, the patient returned to the medical clinic, with the following history. About a year previously, soreness appeared in the left side of the neck, "like taking a cold in the neck." It lasted only a few days, but it reappeared nine months later, in February 1943. She used a liniment, and the pain again disappeared only to recur in two months. With the onset of this pain a "knot" also appeared in the left side of her neck, two days after dental work had been done. During the next four weeks it neither increased nor receded.

The family history was essentially noncontributory. The patient's mother and father were living and well. Three brothers died early in infancy, one brother died of injuries. One brother was living and well. There was no past history of any serious illness in the immediate family.

The patient was born in Georgia Dec. 10, 1908. She had been married for fifteen years. Her husband was living and well. There was one pregnancy, and her only son, aged 13 years, was living and well. She worked as a maid and used tobacco and alcohol in moderation. Occasional constipation was treated with

infusion of senna with magnesium sulfate Acetylsalicylic acid was taken infrequently for headaches or any pain

The past history was noncontributory except for measles and mumps in childhood and the symptoms mentioned previously The blood pressure was as follows 200 systolic and 130 diastolic in the left arm and 190 systolic and 124 diastolic in the right arm The temperature was 98 F and the pulse rate 80, and the respirations numbered 20 per minute

The patient appeared to be a well nourished, slender woman 35 years old and was seemingly in good health The skin was of fine texture, and no abnormalities were seen The hair, bones, joints and muscles appeared normal There was a small, palpable, lymph node in the right cervical region and also an enlarged one in the left supraclavicular area, about 2 cm in diameter, just above and behind the midportion of the left clavicle It was indurated, nontender and freely movable The eyes were normal except for a grade I sclerosis of the arterioles on ophthalmoscopic examination The nose, ears and throat were normal Three teeth were missing, no pyorrhea or other infection was present The thorax and lungs revealed no abnormalities The cardiac findings were reported as follows "The apex pulse is located 10 cm from the midline in the fifth interspace The heart is enlarged to the left and extends 11 cm from the midline in the fifth interspace There is no thrill, the sounds are of full quality and the rhythm is regular There is a grade I blowing systolic murmur heard best just to the left of the sternum in the third interspace The aortic sound is tambor-like"

The abdominal and pelvic findings were normal The results of neurologic examination were normal The laboratory findings on May 26, 1943 were as follows As to the blood, the red blood cells numbered 4,290,000 and the white blood cells 5,200 The hemoglobin content measured 114 Gm (73 per cent) The differential count revealed basophils 1, eosinophils 1, polymorphonuclears 62, lymphocytes 34 and monocytes 2 The urinalysis gave normal results On June 4, 1943, the red blood cells numbered 4,200,000 and the white blood cells 8,200 The hemoglobin content measured 98 Gm (63 per cent) The differential count revealed 56 polymorphonuclears, 32 lymphocytes, 7 eosinophils and 5 monocytes The Kahn reaction of the blood was negative A roentgenogram of the chest showed a heart somewhat enlarged to the left and aortic in type Both pulmonary fields were clear There was no evidence of mediastinal or hilar adenopathy

On July 13 the differential cell count of the blood was substantially the same, barring a reduction to 4 eosinophils Again, the examination of the urine resulted negatively

On July 15, 1943 the glands in the left cervical area were dissected An attempt was made to remove the entire mass of matted nodes, but it was impossible owing to the extensiveness of the process During the manipulation, one of the nodes was broken and caseous material escaped A portion of the mass was removed for biopsy, the report of which was tuberculous adenitis In August 1943, the patient was again examined and no change was found The glandular enlargement was the same

The patient disappeared from observation until May 16, 1944 She stated that following the operation the original nodule remained the same for about three months Afterward, it began to grow It reached a considerable size, burst and has been draining since In January 1944 a private surgeon removed a large part of the mass, following which a draining sinus has persisted In addition, there were numerous large indurated areas in the left side of the neck The left breast was extremely tender, its lower two thirds were homogeneously swollen, and the areola was thick The surrounding skin was atrophic and shiny At about

10 o'clock and 3 cm from the nipple, there was an extremely hard and tender spot. Over the upper portion of the breast there was an infiltrated cutaneous nodule, and a few were present over the anterior wall of the chest. The left arm was slightly swollen, especially around the elbow. In the left axilla numerous fairly soft, slightly elevated nodules were present. An enormous, soft node was present in the left side of the neck, just below the ear. Several enlarged nodes were present in the submaxillary and sublingual regions. Many hard discrete nodes were present at the base on the right side of the neck.

The laboratory findings resulted as follows. The red blood cells numbered 3,450,000 and the white blood cells 23,500, the hemoglobin measured 52 per cent. In the differential count, the polymorphonuclears were 80 per cent, lymphocytes 9 per cent, monocytes 3 per cent, basophils 1 per cent and eosinophils 7 per cent. Polychromatophilia and a certain degree of anisocytosis and poikilocytosis were present. The urinalysis gave normal results.

A biopsy was performed on one of the nodules on the chest on May 17, 1944. The report was as follows: "Sections reveal a peculiar granulomatous condition of the dermis. It bears considerable resemblance to Hodgkin's disease but does not seem to be that disease. The lesions are both circumscribed and diffuse. The cells are chiefly fibroblasts and epithelioid cells. Among these there are many lymphocytes, macrophages and giant cells. Some of the latter resemble foreign body giant cells, whereas others are more like tumor cells. They contain from 4 to 10 nuclei. Again, numerous eosinophils may be seen. Sternberg-Reed cells are not noted. This does not look like a lymphoma of any type. It is some peculiar sort of granuloma. No specific organisms can be found."

On August 16 filtered roentgen ray therapy was administered over the left supraclavicular area, over the left axilla and over the lesions on the chest. The exposures given were 100 r units about every four days. Filtration of 35 mm of aluminum was used at 190 kilovolts and 8 milliamperes. In spite of this treatment, the condition became progressively worse, and on Aug 28, 1944 the patient presented decided edema and elevation of temperature of the right breast. Numerous nodules on the left side of the chest became greatly enlarged and ulcerated. Roentgen ray treatment of the right breast was begun, and the swelling began to subside. The larger nodular lesions on the left side of the chest became more numerous and ulcerated. A photograph was taken at this time. The roentgen ray therapy was continued, and from this date the lesions began to improve gradually but some of the small, deep nodules continued to increase in size and ulcerate. The treatment was continued until September 25. On this date the areas involved received a total dosage which varied from 5,000 to 6,000 r units of filtered radiation (35 mm of aluminum). On Oct 16, 1944 the patient returned for a check-up and seemed much improved. A blood cell count resulted as follows. The white blood cells numbered 9,800. In the differential count, the polymorphonuclears were 39 per cent, lymphocytes 7 per cent, monocytes 6 per cent, basophils 2 per cent and eosinophils 51 per cent.

The condition remained stationary, and on Dec 20, 1944, the patient was referred to the dermatology clinic. The dermatologic findings were as follows. Both breasts were hard and infiltrated and pitted on pressure. The impression was that of considerable fibrosis with edema. Radiation changes were present on the skin of both breasts. On the upper half of the left breast there were numerous deep subcutaneous nodules, 2 mm to 2 cm in diameter. They seemed to be attached to the deep tissues. The skin was movable over the nodules. The older nodules were larger and elevated above the level of the skin. The overlying skin was inflamed but intact except for desquamation over a few. The largest nodules,

which apparently were of the longest duration, appeared in two forms. First, a few 3 to 4 cm in diameter were inflamed and hard, the skin was not movable over them and appeared atrophic. Second, numerous lesions 1 to 4 cm in diameter were hard and infiltrated, and the center was ulcerated. The ulcer was punched out, crateriform and covered by a thin serous exudate or crust. When the crust was removed the base was red and raw. The nodules extended laterally to the left



Fig 1—A, the lesions at their height, at the front of the chest B, lesions on the back

wall of the chest and posteriorly to the left scapula. On the back, several large ulcerated nodules were present. Between the large nodules numerous small ones, 1 to 2 mm in diameter, were present, capped by a soft seborrheic-like scale, which was easily removed. When the scale was removed, a shiny dry papule was exposed. The papules were so numerous and so closely set that in some areas

they fused into plaques. When the scales were rubbed off, the individual papules, as described, stood out clearly. The cutaneous lesions were nontender and not painful.

The patient was hospitalized. She had a constant fever, with an irregular temperature curve, mostly between 100 and 103 F.

A pitting edema appeared in both upper extremities, extending from midarm to the wrist and also on the mons pubis and left thigh. A generalized lymphadenopathy was present, the nodes being discrete, firm and freely movable. Those on the left side of the neck were definitely tender. The nodes showing the greatest enlargement were the submental, right axillary, right inguinal and right epitrochlear. The veins of the neck were distended. The observations on examination of the chest were normal. A firm, nodular mass 5 to 6 cm in diameter was present in the left fornix. Other findings were essentially normal.

The laboratory findings at this time were as follows. The Kahn reaction of the blood was negative, and routine tests of the urine resulted normally. The red blood cells numbered 4,200,000 and the white blood cells 50,900. The hemoglobin content measured 12.2 Gm. The polymorphonuclears were 23 per cent, lymphocytes 3 per cent, and eosinophils 74 per cent. On Dec. 28, 1944 the white blood cells numbered 50,000. In the differential count, the polymorphonuclears were 15 per cent, lymphocytes 1 per cent and eosinophils 84 per cent. On Jan. 9, 1945 the white blood cells numbered 60,600, with a differential count of polymorphonuclears 18 per cent, lymphocytes 5 per cent, monocytes 2 per cent and eosinophils 75 per cent. The examination of the stool gave normal results. The nonprotein nitrogen content measured 25 mg. and the cholesterol content of the blood 130 mg. Roentgen examination of the chest showed no appreciable changes. There was no enlargement of the hilar shadows. There were no changes in the bones.

A biopsy was performed on an inguinal node and the report on the microscopic examination was as follows: "No normal lymphoid tissue is seen. Most of the tissue is fibrous, with a great many lymphocytes of various types present. Most of these are large cells. Numerous multinucleated cells of the Sternberg-Reed type are present. There are innumerable eosinophils present elsewhere. Histologically, this is an instance of Hodgkin's disease."

A biopsy specimen of another cutaneous nodule was sent to Dr. Fred D. Weidman, who reported as follows: "The surface of the lesion is superficially ulcerated. In the corium, a rounded nodule of peculiar granulation tissue appears, which extends to the deepest parts of the skin. Various kinds of cells are disposed on a delicate fibrous reticulum which has replaced entirely the normal collagenous structure. Most conspicuous are the enormous numbers of eosinophilic polymorphonuclears, but an equal number of neutrophils is intermixed. However, suppuration is not indicated at any place. From place to place, a few large monocytes are discoverable, and sometimes they are concentrated into a given area but still remain isolated. They are multinucleate and conform to Sternberg-Reed cells, barring the extreme rarefaction of their cytoplasm and their indefinite outlines. The nucleus is usually degenerated, and, accordingly, these cells should be regarded as being in a state of hydropic degeneration. The fibrosis of the reticulum which is usual in Hodgkin's disease is scantily developed. Blood vessels ramify richly through the infiltration, they are frequently dilated and engorged by eosinophilic polymorphonuclears." Dr. Weidman was unwilling to make a final diagnosis of Hodgkin's disease at this time.

*Summary of History of Case*—Over a period of at least three (and, doubtless, more) years, deep and ulcerated granulomas developed in the lymph nodes and



Fig 2—Early granuloma of the skin, illustrating the large clear cells that are regarded as monocytes. The eosinophilia was not so extreme in this region as at others. Polymorphonuclear neutrophils are numerous. Sternberg-Reed cells did not appear in early lesions such as this one was.

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skin of a 35 year old Negro woman. They began in the left side of the neck, and although they were concentrated on the upper left side of the thoracic wall they finally extended to the right breast. Eventually, a generalized lymphadenopathy appeared and attacks of fever. Anemia gradually developed (as low as 3,450,000 red blood cells and with a hemoglobin content of 52 per cent), together with an eosinophilia (absent at first), which finally reached 84 per cent. There was not any evidence of enlargement of the liver and spleen. Extremely heavy doses of roentgen rays resulted in definite but only temporary benefit. The histologic processes in the skin were not diagnostic for any entity, at first there was not any tissue eosinophilia, but eventually it became extreme indeed. The diagnosis of Hodgkin's disease was delayed because the histologic picture remained atypical for a long time, and was clinched only when a biopsy of a lymph node was performed.

#### HISTOPATHOLOGY

Altogether, five specimens of skin and two of lymph nodes were studied. The largest lesion from the skin measured 2 cm. in diameter and the smallest 0.5 cm. It was thus possible to study the disease in, both young and old lesions and to learn that there was considerable variation in the two. Inasmuch as eosinophilic granuloma is a new arrival in dermatology, it is proper to record the pathologic processes in detail, whether it proves to be a separate entity or not. Moreover, with five specimens of skin at hand, an unusual opportunity was afforded to learn something of the range of histologic changes that are possible in Hodgkin's disease (as in young and old lesions).

*Skin.* When ulceration was present, regeneration was highly developed at the margins, amounting almost to pseudoepitheliomatous hyperplasia. Even in early lesions, the epidermis was definitely acanthotic (and edematous). This was to be expected when such large masses of polymorphonuclears were present in the corium, because products of degeneration which must be developed in such extreme leukocytic processes can diffuse into the epidermis and produce a hyperplasia of its cells. This would be the case whether the leukocytic hyperplasia is fundamental to the Hodgkin's disease in this case or not.

It was in the corium, though, that the significant processes occurred. In early lesions, diffuse masses of special granulation tissue replaced all the normal structures. The stroma was delicately reticular and did not include any definite fibrous tissue strands, such as are so useful in the diagnosis of Hodgkin's disease. The infiltrative cells were nearly equally divided between lymphocytes and polymorphonuclears, together with small numbers of monocytes and numerous atypical Sternberg-Reed cells. Goodly numbers of capillaries ramified regularly through the infiltration, their walls were thick because their endothelial cells were hyperplastic and swollen. In one specimen they were highly dilated and engorged by eosinophilic polymorphonuclears. The tissue eosinophils comprised an estimated 50 to 75 per cent of all the polymorphonuclears.

and at some places had accumulated into masses comprised almost solely of such cells. The Sternberg-Reed cells were numerous and tended to accumulate in certain localities. They were not typical, although they were sometimes multinucleate, their cytoplasm was highly rarefied and reticular, and their outlines were indefinite. Indeed, it was not certain that they were in fact such cells until the biopsy of the inguinal node disclosed the typical ones.

In older lesions, the cellular infiltrative mass became broken up into irregularly shaped areas, the patterning of which suggested that they were arranged in interlacing, broad, most irregularly shaped tracts or bundles that were reminiscent of the patterning of sarcoma (the so-called Hodgkin's sarcoma?). Now, lymphocytes comprised a moderate majority of all the cells. A smaller percentage of the polymorphonuclears was eosinophilic, estimated at 30 to 40 per cent, and indeed in one specimen they were limited to a few widely scattered but still sizable aggregations. A few strands of young fibrocellular tissue could now be discovered at widely separated positions, thus adding an important item in the diagnosis of Hodgkin's disease. Blood vessels became definitely reduced in numbers. Sternberg-Reed cells were also relatively few and had changed from the rarefied form to one with a solid cytoplasm and a definite outline. Histiocytes now dominated the picture, with the result that the eosinophils and lymphocytes appeared to be scattered at intervals by contrast with the density with which they occurred in the early lesions. They were outstandingly spindle in shape and, occurring as they did in bundles, contributed to the resemblance to sarcoma that was previously mentioned.

*The Lymph Nodes*—In a specimen from a "caseated" node, the architecture of lymph node could not be identified, evidently the lesion had become so large that only a part of it was submitted for microscopic examination. It consisted mostly of adult fibrous tissue, within which various foci of cellular infiltration were located. In them, lymphocytes and polymorphonuclears were present in approximately equal numbers, the latter tended to occur in small, ill defined foci. Eosinophils were few and widely scattered. Monocytes were relatively few. The Sternberg-Reed cells were abundant and typical. The large numbers of polymorphonuclears being barred, the picture was typical for Hodgkin's disease.

A second specimen likewise came from a large node, but it is not known whether it had undergone caseation. In any event, a young cellular fibrosis was developed throughout the section and the Sternberg-Reed cells were numerous and typical. With these two exceptions, the picture was of the order of that exhibited in early cutaneous lesions. That is the lymphocytes and polymorphonuclears were numerous indeed and were present in approximately equal numbers, many of the latter

were eosinophilic, and monocytes were relatively few. Moreover, a few of the latter had the large, clear cytoplasm and indefinite outlines that were described previously in early lesions of the skin.

The rarefaction of the Sternberg-Reed cells prompted a test for fat, but tissue from the lymph nodes alone was available for frozen sections. Sudan III preparations did not disclose fat in them, but there were great numbers of minute globules free in the tissue spaces and small numbers in the monocytes. Typical foam cells were not developed though, the general form of the monocyte was preserved, and it was swollen only slightly.

*Analysis of the Histologic Changes.* Hodgkin's disease will be dealt with first. The full complement of diagnostic criteria appeared only in the lymph nodes and in the older examples of cutaneous lesions. For the skin, particularly at fault was the development of fibrosis and of unequivocal Sternberg-Reed cells, indeed, early lesions exhibited no fibrosis, and Sternberg-Reed cells were few and atypical. The number of monocytes varied widely, in fact, they were numerous in only one of the older cutaneous lesions (the one described as sarcomatoid in its patterning).

The ensemble speaks for varying degrees in acuteness (speaking in terms of tissue processes) of the Hodgkin processes. For the skin, acuteness is indicated by the absence of fibrosis and by the rarefied (hydropic) type of Sternberg-Reed cell, and it must be added that the latter cells were also represented in the actively proliferative part of one of the lymph nodes. Second, the picture speaks for tardiness in the development of the more chronic (mature and more diagnostic) features in the skin. This is in keeping with clinical knowledge that the cutaneous expressions are dominantly nonspecific (urticaria and similar conditions), it is seldom that typical granulomatous lesions of Hodgkin's disease are observed in the skin, and the dermatopathologist, too, seldom observes the same, and typical, picture that he is so familiar with in the lymph nodes. In the light of this case, even though the cutaneous lesions were of many months' duration, the processes in the skin remained young and immature in type, they did not nearly approach those of the lymph nodes. This intimates, once again, that certain forces are operative in the skin (immunologic?) which are not operative at least in the lymph nodes and perhaps in other tissues. Incidentally, Tuft<sup>1</sup> approached this topic when he demonstrated that typhoid agglutinins were more highly developed after injections into the skin than after intravenous ones.

This case, then, assists in the arrival at the following generalizations in respect to Hodgkin's disease. It is tardy in affecting the skin if it

1 Tuft, L. The Skin as an Immunological Organ, with Results of Experimental Investigations and Review of Literature, *J. Immunol.* 21: 85 (Aug.) 1931.

does so at all. When it does involve the skin, the lesions are usually non-specific, histologically as well as clinically. In the rare cases in which granulomatous lesions develop, the tissue reaction is relatively acute in type, seldom indeed does the final, fibrous reaction occur such as is so familiar in the lymph nodes. 'One of us (F. D. W.) has studied a case in which the patient at necropsy had great numbers of cutaneous nodules. For years, these lesions had been regarded as various diseases, including psoriasis and seborrheic dermatitis. She had been presented, too, at a meeting of the Chicago Dermatological Society, but Hodgkin's disease was not suspected. The typical histologic picture was not exhibited in any of the several nodules examined. The cellular infiltrate consisted almost entirely of lymphocytes. Moderate numbers of monocytes represented the most that could be construed in favor of Hodgkin's disease. Incidentally, their cytoplasm, too, were highly hydropic and their outlines indefinite.

The histopathology will be discussed next from the standpoint of the eosinophilia and eosinophilic granuloma. Tissue eosinophilia was just as extreme in the "acute" lymph nodes as in the skin but was not as spectacular, because the fibrous matrix diluted, so to speak, all the infiltrative cells. They thus became scattered over a wider area, they were not condensed, as in the skin. Still, the proportion of eosinophils to neutrophils and to monocytes was just as high as in the skin. That is, the eosinophilic response per se was as great in the lymph node. Incidentally, whether the eosinophilic leukocytes bespeak an acute type of reaction or not, the neutrophils must. The nuclei were almost invariably bilobate or multilobate and could not be interpreted as eosinophilic myelocytes.

What is the significance of the eosinophilia in our case? The simplest explanation is that the Hodgkin's disease was complicated by some general eosinophilogenic condition such as trichinosis, hookworm disease or allergy. In such case, the superabundant eosinophils of those diseases would be represented by eosinophilia in the tissue reaction of the Hodgkin lesions. The second theory would concern hemopoietic tissue, in the direction of the myelocytes and monocytes particularly. The literature on eosinophilic granuloma of the skin is replete with discussion centering around eosinophilic myelocytes, and that on eosinophilic granuloma of bone naturally revolves around the hemopoietic tissue in bone marrow. In short there may be a common ground for the two eosinophilic granulomas (bone and skin) and Hodgkin's disease through the medium of hemopoietic tissue.

At this juncture, the introduction of fat into the picture in our case brings Letterer-Siwe disease into the case. By now, it appears to be the consensus that Hand-Christian disease, Letterer-Siwe disease and eosinophilic granuloma of bone are members of the same fundamental

disease processes. The latter are best known as they are seen in Hand-Christian disease and have to do with a monocytic hyperplasia which is attended by lipidal infiltrations. The details cannot be discussed here, suffice it to point out that in our patient both the monocytic and the fatty changes were represented. If it should develop in the future that eosinophilic granuloma of the skin qualifies as an entity when the eosinophilia is combined with some leukosis (including monocytic disease like Hodgkin's disease), our case would automatically qualify as one of eosinophilic granuloma, and all cases of Hodgkin's disease would fall into that category when they were accompanied with eosinophilia. This thinking is too extreme in the present state of our knowledge, and, accordingly, our case should be regarded for the present simply as one of Hodgkin's disease, but with an extraordinary degree of eosinophilia.

#### CONCLUSIONS

In Hodgkin's disease, granulomatous lesions are relatively rare in the skin. They develop tardily and incompletely compared with those in the lymphadenoid tissues.

It would appear that in the initial stages the tissue reaction in the skin is far more acute in type than that in the lymph nodes, perhaps more acute than ever occurs in the lymph nodes, and in our case the extreme polymorphonuclear neutrophil reaction was particularly significant. The fibrosis and the development of Steinberg-Reed cells are so seldom exhibited in the skin that the dermatopathologist is denied this assistance in diagnosis in a way that is not the case for the general pathologist. Lymph nodes are far more promising leads toward histologic diagnosis than the skin.

The extraordinary eosinophilia in our case may or may not be significant for an interrelationship with eosinophilic granuloma. It remains to be demonstrated whether the scope of Letterer-Siwe disease is sufficiently broad genetically to include Hodgkin's disease, but the demonstration of fat in a lymph node of our patient may be significant.

# TREATMENT OF VARIOUS TYPES OF CUTANEOUS TUBERCULOSIS WITH PROMIZOLE AND STREPTOMYCIN

A Preliminary Report

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**T**HIS preliminary report on treatment of certain types of cutaneous tuberculosis and tuberculids is part of a study of various agents in the treatment of tuberculosis that was started several years ago by two of us (Feldman and Hinshaw)<sup>1</sup> This report deals with the clinical application to cutaneous tuberculosis of promizole<sup>2</sup> and streptomycin,<sup>3</sup> which were found to be the least toxic and have demonstrated the greatest therapeutic effect of any of the substances which were used in treatment of tuberculous guinea pigs

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1 (a) Feldman, W H, Hinshaw, H C, and Mann, F C Effects on Experimental Tuberculosis of 4,2'-Diaminophenyl-5'-Thiazolesulfone (Promizole) Preliminary Report, Proc Staff Meet, Mayo Clin **19** 25-33 (Jan 26) 1944 (b) Feldman, W H, and Hinshaw, H C Effects of Streptomycin on Experimental Tuberculosis in Guinea Pigs Preliminary Report, *ibid* **19** 593-599 (Dec 27) 1944 (c) Hinshaw, H C, Feldman, W H, and Pfuetze, K H Clinical Administration of 4,2'-Diaminophenyl-5'-Thiazolesulfone (Promizole) in Tuberculosis Preliminary Report, *ibid* **19** 33-36 (Jan 26) 1944 (d) Feldman, W H, Hinshaw, H C, and Mann, F C Streptomycin in Experimental Tuberculosis, Am Rev Tuberc **52** 269-298 (Oct) 1945 (e) Hinshaw, H C, and Feldman, W H Streptomycin in Treatment of Clinical Tuberculosis A Preliminary Report, Proc Staff Meet, Mayo Clin **20** 313-318 (Sept 5) 1945

2 Supplied by Dr L L Bambas and Dr E A Sharp, Parke, Davis & Company, Detroit

3 Supplied by Dr D F Robertson and Dr J M Carlisle, of Merck & Co, Inc, Rahway, N J, and by Dr George Hazel, of the Abbott Laboratories, North Chicago, Ill

Since Ehrlich\* developed the satisfactory arsenical for treatment of syphilis, a constant search has been made for some similarly effective agent for the treatment of tuberculosis. Although results with use of metallic substances have been unsuccessful, with the advent of the sulfonamide compounds, the sulfones and, shortly afterward, the antibiotic agents, investigation in this field was stimulated again.

Rich and Follis,<sup>4</sup> in 1938, were the first to report on the influence of sulfanilamide in treatment of tuberculosis in guinea pigs. They reported that retardation in the development of tuberculosis in guinea pigs was observed, although the drug did not in any instance arrest the disease. The drugs of the sulfone series, promin (sodium p,p'-diaminodiphenylsulfone-N,N'-dixetrose sulfonate), diasone (disodium formaldehyde sulfoxylate diaminodiphenyl sulfone) and promizole (4,2'-diaminophenyl-5'-thiazolylsulfone), were found actually to arrest tuberculosis in infected guinea pigs, however, enthusiasm has decreased because on clinical use in many cases minimal therapeutic effect was noted and varying degrees of toxic reactions were encountered.

With the introduction of penicillin, hope was again revived that the course of tuberculosis could be altered by a specific substance, however, penicillin was found to have no effect against the disease. Nonetheless, continued efforts revealed that other substances that could be extracted from living micro-organisms were able to suppress growth of bacteria which produce disease. The most outstanding of these substances are streptothricin and streptomycin, which were discovered by the group of investigators who worked with Waksman.<sup>5</sup> Both are derived from soil-inhabiting fungi (*Actinomyces lavendulae* and *Actinomyces griseus*) and have the ability to inhibit the growth of *Mycobacterium tuberculosis* in test tubes. Streptomycin is well tolerated by guinea pigs, and in about a third of the animals it will eradicate advanced tuberculosis. In the majority of the remaining two thirds, the disease may be regarded as arrested after its use.<sup>1b</sup> Streptothricin is toxic to guinea pigs, and its influence on tuberculosis is less favorable than that of streptomycin.

We have treated 15 patients who had various forms of cutaneous tuberculosis, consisting of lupus vulgaris, scrofuloderma, tuberculosis cutis colliquativa, erythema induratum, primary inoculation tuberculosis, tuberculosis miliaris disseminata faciei and papulonecrotic tuberculids. Eight of the 15 patients received promizole, and 7 received

4 Rich, A. R., and Follis, R. H., Jr. The Inhibitory Effect of Sulfanilamide on the Development of Experimental Tuberculosis in the Guinea Pig, *Bull. Johns Hopkins Hosp.* **62**: 77-84 (Jan.) 1938.

5 Waksman, S. A., Bugie, E., and Schatz, A. Isolation of Antibiotic Substances from Soil Micro-Organisms, with Special Reference to Streptothricin and Streptomycin, *Proc. Staff Meet., Mayo Clin.* **19**: 537-548 (Nov. 15) 1944.

streptomycin, 3 of the patients who had received promizole first were treated subsequently with streptomycin. Of the 15 cases, only 12 will be reported in this paper.

#### PROMIZOLE

Promizole was synthesized first by Bambas<sup>6</sup>. The average dose for adults is 8 to 16 Gm per day, and it is administered orally. In our cases the larger doses in this range occasionally produced toxic reactions, which were minimized considerably when the dose was reduced to 8 or 10 Gm daily. When this dose was administered each day for periods ranging from approximately six weeks to four months, from 500 to about 1,200 Gm of the drug was given. The following reports of 4 cases illustrate the effect of promizole on scrofuloderma, lupus vulgaris and erythema induratum.

**CASE 1—*Scrofuloderma***—A white woman 49 years of age began to have suppurative cervical adenitis on the left side in April 1941. After that, similar lesions had developed in the cervical and axillary regions on the right side. Many of the glandular abscesses had been incised, and others had ruptured spontaneously. All had persistent draining sinuses. The patient had lost 20 pounds (9.1 Kg) in two years.

Roentgenologic examinations of the chest gave negative results. Material from a sinus in the cervical region was used for the inoculation of guinea pigs, which subsequently gave positive reactions for Myco tuberculosis. The tuberculin test performed with first strength purified protein derivative elicited a positive reaction. The sedimentation rate was 118 mm per hour (Westergren method).

Treatment with promizole was begun on Dec 22, 1943. The patient received approximately 500 Gm in the following four weeks, and some clinical improvement was believed to have occurred during this time. The drug, however, produced some nausea and anorexia. The level of hemoglobin dropped 1 Gm during administration.

The patient has since reported that no significant improvement has occurred.

**CASE 2—*Lupus vulgaris***—A white woman 62 years of age had had an erythematous infiltrated plaque involving the left ala, septum and bulb of the nose three years previous to her admission to the clinic in August 1944. Several small apple jelly nodules were found on diascopy. A biopsy specimen revealed the typical architecture of lupus vulgaris, but no tubercle bacilli were seen in the section.

The patient's general health was good. Roentgenologic examination of the chest gave negative results, and the routine laboratory findings were within normal ranges.

A total of 1,250 Gm of promizole was administered in four months, being started on Aug 8, 1944. The drug was well tolerated except for slight anorexia late in the period of treatment.

No significant improvement was observed in this period of treatment.

6 Bambas, L. L., cited by Feldman, W. H., Hinshaw, H. C., and Mann, F. C. Promizole in Tuberculosis. The Effect on Previously Established Tuberculosis of Guinea Pigs of 4,2'-Diaminophenyl-5'-Thiazolylsulfone (Promizole), *Am Rev Tuberc* 50 418-440 (Nov) 1944.

CASE 3—*Erythema induratum*—A white woman aged 37 years had had recurring crops of discrete ulcerative lesions low on the anterior and medial aspects of the legs for twenty years prior to her admission to the clinic in January 1944. The lesions had been painful, discrete nodules, which ulcerated and eventually healed, leaving an atrophic pigmented scar. The lesions had occurred chiefly in the summer months.

At the time of admission, several ulcers were present and a zone of infiltration measured 1 inch (2.5 cm) in diameter (fig 1a). A biopsy specimen revealed erythema induratum. Cultures of the specimen removed and results of examinations of inoculated guinea pigs were negative for *Mycobacterium tuberculosis*. The sedimentation rate was 30 mm per hour (Westergren). The patient's general health was good. The Mantoux test elicited a positive reaction, but a roentgenogram of the chest was negative for tuberculosis.



Fig 1 (case 3)—*Erythema induratum*. a, Jan 1, 1944, b, healed lesions after treatment with 750 Gm of promizole. The patient remained well for more than a year, when the lesions recurred.

Treatment with promizole was started on Jan 12, 1944 and was continued for six consecutive weeks. A total of about 500 Gm was given. The ulcerations were judged to be about half healed at the end of this time.

She returned in June 1944. In one month during this interval she had taken approximately 250 Gm of promizole. At the time of the patient's return the ulcers were all healed, and they remained so during the entire summer (fig 1b) and the following winter. This was remarkable for this patient, as she always had had the lesions during the summer months.

In September 1945, the patient reported that several small ulcers had recurred on each leg.

CASE 4—*Sicofuloderma*—This patient, a white man 33 years of age, stated that suppurative adenitis had begun in the cervical and axillary regions in 1942. The affected lymph nodes ultimately had ruptured, ulcerated and produced persistently draining sinuses. The patient had lost about 30 pounds (13.6 Kg). About six months after the onset of the adenitis (May 1943) an inflammatory condition of the left eye had developed.

The patient presented himself for examination at the clinic on Jan 11, 1944, at which time multiple draining sinuses were noted around the neck and in the axillas. Guinea pigs were inoculated with exudate obtained from some of the sinuses, and evidence of tuberculosis was found on examination of the animals. A tuberculin test in which first strength purified protein derivative was used gave a positive result. The sedimentation rate ranged from 6 to 22 mm per hour (Westergren). A roentgenogram of the chest was normal.

A diagnosis of tuberculous iridocyclitis was made by the consultants in the section on ophthalmology. Administration of promizole was begun on Jan 14, 1944, with a dose of 16 Gm daily and was continued for three months. At intermittent intervals thereafter, 500 Gm of promizole per course was given until November 1944. At that time oral administration of promizole was discontinued and was replaced by topical application of powdered promizole to the ulcers and into the draining sinuses. Topical application was continued until February 1945.

The ulcers and most of the sinuses healed, and the inflammation of the eye subsided by July 1944. A few sinuses persisted in the axillary regions at the time the patient was dismissed from the clinic, in February 1945. Subsequent reports from the patient as late as February 1946 revealed that improvement had been maintained up to that time, although occasionally a new abscess developed around the cervical region. He had gained about 25 pounds (11.3 Kg).

#### STREPTOMYCIN

Streptomycin usually was given in doses of approximately 1,000,000 units per day as a streptomycin salt in an aqueous solution. At present 1,000,000 units of streptomycin is referred to as 1 Gm. Approximately 125 mg was injected intramuscularly every three hours throughout the twenty-four hours. One patient received 2 Gm daily for a few weeks, but this dose was discontinued because the patient complained of nausea, lassitude and general debility. In general, however, the drug was of low toxicity and was tolerated well by the majority of the patients. Early in the production of streptomycin some inadequately purified materials produced febrile reactions and histamine-like headaches soon after injections, but these reactions were eliminated when purified preparations were made available. The total doses per course of treatment varied from 15 to 128 Gm. In 3 cases in which treatment was given soon after the introduction of streptomycin, the smaller doses per course were given. A relapse occurred within a short time in these cases, and hence it was thought that the smaller total doses per course were inadequate. Some of these patients were given a second course, in which the larger total dose averaged about 60 Gm. Some patients who were treated later received as much as 128 Gm in a continuous program.

As streptomycin was not always available, it was necessary in some cases to discontinue treatment when our supply was exhausted. Even though we realized the value of larger doses, such as 2 Gm a day, it was not always possible to give these doses for a long period.

The following reports of 5 cases illustrate the effect of streptomycin in cases of scrofuloderma, tuberculosis miliaris disseminata faciei and tuberculosis cutis colliquativa

CASE 5—*Scrofuloderma*—A white man 60 years of age had begun to have a series of suppurative processes in the lymph nodes in the cervical and submaxillary regions in 1943. Multiple draining sinuses had subsequently developed from these lesions. Efforts at surgical excision had been unsuccessful, and no tendency to healing was observed prior to treatment at the clinic.

The patient's general health had been good. He had lost only 8 pounds (3.6 Kg). Roentgenologic examination of the chest gave negative results. Inoculation of a guinea pig with material from a cervical abscess gave positive evidence of *Myco tuberculosis*.

Treatment with streptomycin was begun in July 1945, and the patient received 21.5 Gm of streptomycin in five weeks. The course was interrupted briefly because a febrile reaction occurred from impurities from one lot of the drug. The drug was well tolerated after subsequent resumption of treatment with a different lot. At the end of this course of treatment, drainage from the sinuses had stopped and the inflammatory reaction of the abscesses was reduced materially.

A few months later the patient commenced to lose weight. Tuberculous peritonitis developed later, and he died elsewhere eight months after treatment with streptomycin was stopped.

CASE 6—*Scrofuloderma*—The patient, a white man 21 years of age, registered at the clinic in October 1945. In March 1943, while he was in military service, cervical adenitis had developed for the first time. One of the nodes had been excised and had been reported to be tuberculous. Subsequently, fluctuation, ulceration and persistent draining sinuses developed. Similar lesions occurred in both axillae in the spring of 1945.

Several smears of the secretion from the draining sinuses made at the clinic were negative for *Myco tuberculosis*, but results of inoculations of guinea pigs with material from the same source were positive. Mantoux tests performed elsewhere were reported as giving a positive result.

The patient received the first course of treatment with streptomycin, beginning on Oct 11, 1945. He received 69.0 Gm in fifty-six days. In the course of treatment, the circumference of his neck decreased from 40 to 34 cm and all sinuses stopped draining. Several hard palpable cervical lymph nodes were still present.

On Jan 1, 1946, three weeks after the patient was dismissed from the clinic, however, ulceration recurred at the former sites, axillary sinuses drained again and another axillary abscess developed. A second course of streptomycin was begun on Jan 16, 1946, and the total dose for this course was 73.4 Gm. Most of the ulcers healed, but several of the sinuses were patent but dry when the man was dismissed from the clinic, on April 15, 1946. An oral lichen planus, which was not considered relevant to treatment with streptomycin, developed about this time.

CASE 7—*Scrofuloderma*—A white woman 70 years old registered at the clinic on Dec 16, 1945. Suppurating cervical adenitis on the right side had developed in September 1945. The lesion enlarged rapidly and was incised and drained in October 1945. A large draining ulcer resulted at the site of incision and was still present when she came to the clinic.

A roentgenogram of the chest made at the clinic revealed evidence of emphysema. A tuberculin test to first strength purified protein derivative was positive. Res

of inoculations of guinea pigs with purulent exudate from the surface of the ulcer were positive for Myco tuberculosis, as was a culture of the same material. A smear of material from the surface of the ulcer revealed acid-fast organisms. A biopsy specimen from the edge of the ulcer revealed caseous tuberculosis.

Treatment with streptomycin was instituted on Dec 20, 1945 (fig 2 a), and the patient received 85.5 Gm in eighty-one days. She was dismissed from the clinic on March 12, 1946. At that time the ulcer was about 90 per cent healed. She returned to the clinic in May 1946, and the ulcer was then well healed (fig 2 b).

**CASE 8—*Tuberculosis miliaris disseminata faciei***—In a white woman 32 years of age tuberculosis miliaris disseminata faciei had developed in 1941. She had no symptoms or evidence of pulmonary disease at that time, but four months later a pulmonary hemorrhage occurred. A moderately advanced lesion was then manifest on roentgenologic examination of the chest. This lesion cleared with care at a sanatorium. The cutaneous lesions, however, had persisted without spontaneous remissions for four years.

On admission to the clinic in 1945, biopsy of a cutaneous lesion was performed and the clinical diagnosis made elsewhere was confirmed. A culture of the gastric contents revealed Myco tuberculosis, and an apical lesion of pulmonary tuberculosis of minimal extent had reappeared. The sedimentation rate was moderately elevated. An attempt was made to culture the specimen of the skin, but this was unsatisfactory. The results of two inoculations of guinea pigs were negative.

The patient was hospitalized for six months. In this period three courses of streptomycin were administered. A total of 100 Gm was given. No significant lasting improvement of the cutaneous lesions occurred, although temporary remissions were noted in relation to each of the three courses of treatment. These remissions were followed promptly by relapses when treatment was discontinued. The woman gained 16 pounds (7.3 Kg), her general health improved and a roentgenogram of the chest revealed clearing of the pulmonary infection. We have minimized the effect of treatment on the cutaneous lesions in view of the tendency for this disease to develop spontaneous remissions.

**CASE 9—*Tuberculosis cutis colliquativa, scrofuloderma***—A white man 46 years of age came to the clinic in April 1945. Adenopathy had developed in the right supraclavicular region in 1943. A node was excised for biopsy elsewhere and was reported to be a gumma. The incision failed to heal, and soon a crusted ulcer developed. In the following two years similar lesions had developed in the sternal region and on both sides of the neck. Previous to registration the right axillary nodes suppurated and ruptured spontaneously, and a purulent exudate drained through several sinuses. Antisyphilitic treatment had been administered elsewhere and had been ineffective. There had been no tendency to spontaneous improvement.

In the course of examination of the patient at the clinic, smears made with material from the ulcers and cultures of exudate from various ulcers and sinuses revealed acid-fast organisms of the Myco tuberculosis type. The first strength intracutaneous tuberculin test utilizing purified protein derivative gave a strongly positive reaction. The sedimentation rate was 75 mm per hour (Westergren). A biopsy specimen from an ulcer revealed an atypical tuberculosis cutis colliquativa.

Administration of streptomycin was begun on April 7, 1945. The patient received only 17.1 Gm of the drug in forty-four days. All ulcers were essentially healed at the end of the course of treatment, and the patient gained 5 pounds (2.3 Kg). He was dismissed from the clinic at the end of the course of treatment.

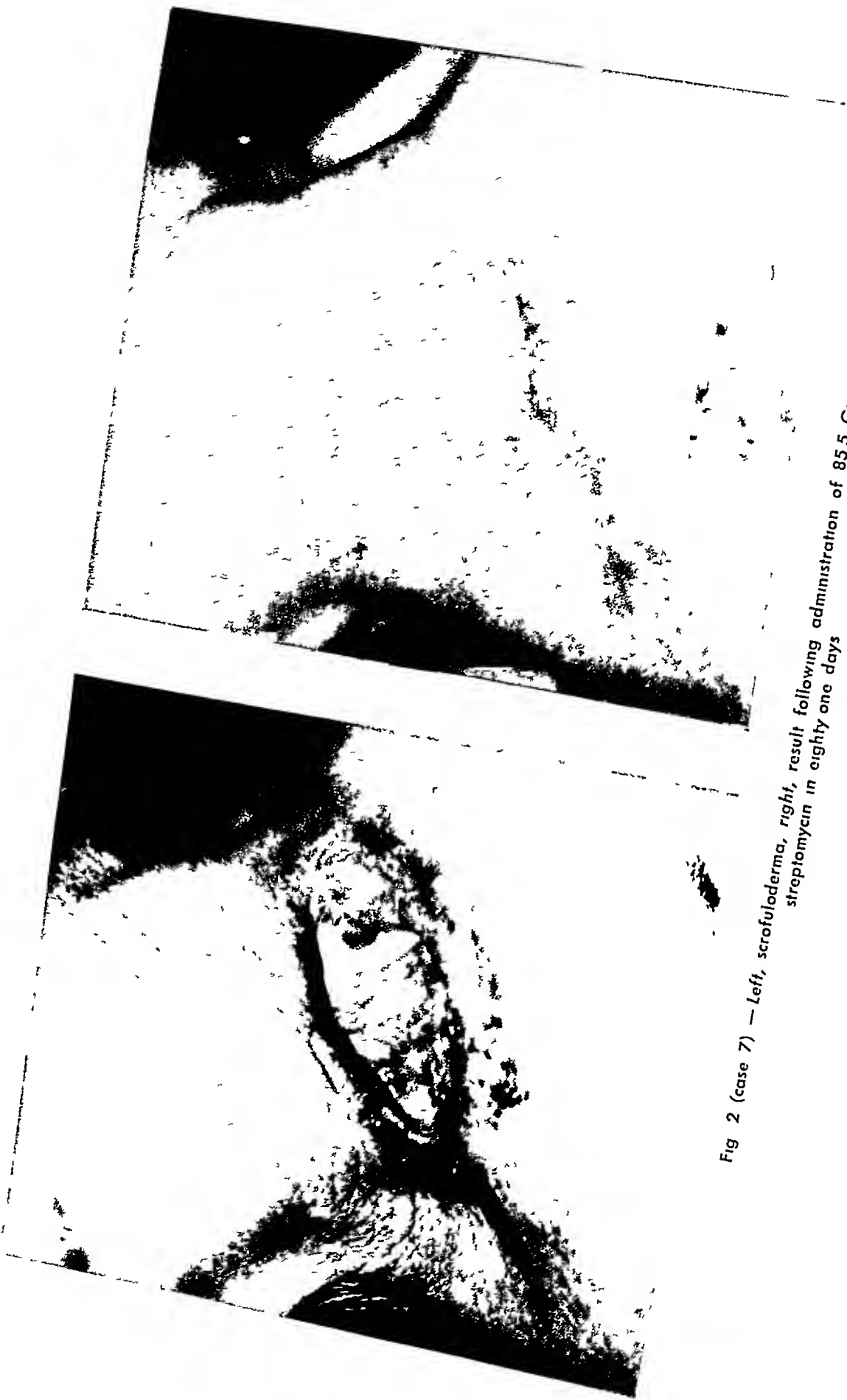


Fig 2 (case 7) — Left, scrofuloderma, right, result following administration of 85.5 Gm of streptomycin in eighty one days





Fig 3 (case 10) — Lupus vulgaris. *Left*, August 1945, *right*, December 1945, healing of the ulceration after administration of 115 Gm of streptomycin. A biopsy specimen on Dec 12, 1945 still shows active tubercles



About a month later the ulcers recurred at the former sites and gradually enlarged, so that in four months, after treatment with streptomycin was stopped, they were the same size they had been on the patient's first admission

A second course of streptomycin was instituted Sept 30, 1945, and the patient received 316 Gm in thirty-five days. Although this course of treatment was regarded as inadequate, 80 per cent of the ulcers had healed when the patient was obliged to return home and the treatment was discontinued. Subsequent follow-up at a recent date revealed that some ulcers were still present and draining

#### PROMIZOLE AND STREPTOMYCIN

In the following 3 cases promizole was given first, and, when results were considered to be unsatisfactory on months of observation, streptomycin was given

CASE 10—*Lupus vulgaris*—The patient, a white woman 48 years old, registered at the clinic in August 1944. She had been found to have tuberculous cervical adenitis in 1930. Cervical adenitis increased and abscesses formed periodically in the following ten years. In 1942 a plaque of infiltrated erythematous dermatitis appeared on the neck. This rapidly progressed in the following two years and extended upward onto the left cheek and lobe of the left ear and downward on the left side of the neck.

In August 1944, the patient presented herself at the clinic, when the large infiltrated plaque just described was observed and the central portion of the plaque was ulcerated and exudative. Diascopy revealed numerous apple jelly nodules. Biopsy revealed that the lesion was typical of lupus vulgaris. An intradermal test with first strength purified protein derivative gave a strongly positive result. The sedimentation rate was 55 to 80 mm per hour (Westergren). When a guinea pig was inoculated with material from the plaque no gross lesions were seen, but cultures of the spleen of the animal were positive for Mvco tuberculosis. The patient was obese, and her general health was good. The roentgenogram of the chest revealed no abnormalities.

From August to November 1944, the patient received 1,400 Gm of promizole. The drug was well tolerated but produced no significant improvement in the cutaneous lesions.

When the patient returned to the clinic on Aug 22, 1945, the lesions had not healed (fig 3a). Treatment with streptomycin was instituted. She was considered to be a suitable candidate for treatment because no tendency to spontaneous improvement had been evident in the observation period of one year. She received 115 Gm of streptomycin in one hundred and seventeen days. In this period, gradual healing of the ulcerative process occurred and considerable involution of the infiltrative quality was noted (fig 3b). However, biopsy performed at the termination of this course of treatment revealed that typical tubercle formation was still present. This was regarded as an indication of latent activity.

CASE 11—*Lupus vulgaris*—A white man 33 years old registered at the clinic. Cervical lymphadenopathy had developed in 1938. Excision of a node from the left side of the neck had resulted in a draining sinus, which had persisted for almost a year. The pathologist had reported that a nonspecific inflammatory reaction was present in the excised node. In 1940 the draining sinus had been excised, and the pathologist had reported that hyperplastic tuberculosis was present in the specimen. A plaque of lupus vulgaris had developed at the site of excision and

gradually had enlarged. Another small plaque developed on the nose in 1942 and one on the scalp in 1943.

In February 1944, when the patient was examined at the clinic, the plaque at the site of excision in 1940 measured 6 by 10 cm and involved the left side of the face and neck. A biopsy specimen from the lesion on the left cheek revealed the pattern of lupus vulgaris. No acid-fast organisms were discernible on microscopic examination of the tissue or on culture. Results of inoculation of a guinea pig were negative.

The patient's general health was good. A roentgenogram of the chest revealed considerable mediastinal widening, which was attributed to adenopathy. The sedimentation rate was only slightly accelerated. The patient was hoarse, and laryngoscopic examination revealed thickening and injection of both vocal cords.

Treatment with promizole was instituted in February 1944 and was continued intermittently until November 1944. Treatment was interrupted several times because the patient did not tolerate the drug or because he was absent from the clinic. For the most part, however, administration was regular for periods of a month at a time. He took 10 to 16 Gm per day. In the period of treatment the lesion was thought to have changed, as the erythematous color faded into a fawn color but no significant involution was apparent.

On April 7, 1945, a course of treatment with streptomycin was begun, and a total of 18 Gm was administered in twenty-four days. During this course of treatment no change was noted in the cutaneous lesions, and no change was noted subsequently. In view of subsequent experience we believe that the patient did not have an adequate amount of treatment.

**CASE 12—*Scrofuloderma***—A white farmer 62 years old came to the clinic in October 1944. His health had been good until September 1943, when some fluctuating abscesses developed in the sternal region. These were incised, but persistent draining sinuses developed. In the following year similar abscesses and subsequent draining sinuses developed in the axillary and cervical regions. Roentgenologic examination of the chest revealed no evidence of tuberculosis. Results of routine laboratory tests were within normal limits. Acid-fast organisms were demonstrated in a stained smear of exudate from a draining sinus in the sternal region, and in guinea pigs that were inoculated with the secretion from several of the draining sinuses tuberculosis developed. One culture of exudate obtained from the axilla was positive for *Mycobacterium tuberculosis*.

Treatment was started on Oct 19, 1944. The patient received 8 Gm of promizole daily for four months. Some reduction in drainage from the sinuses occurred, but no significant healing took place. Administration of streptomycin was begun on April 24, 1945 and was continued for twenty-eight days. The patient received 17.6 Gm of this antibiotic agent in this first course. He remained under observation for two months after treatment was stopped. In this period, several residual draining sinuses healed and some reduction in the inflammatory process of the involved regions occurred.

The patient returned on Sept 12, 1945, three and a half months after the first course of treatment with streptomycin. A large fluctuating abscess had developed in the right axilla. His temperature was 101 F, and he appeared toxicemic and weak. He was hospitalized and was given 31 Gm of streptomycin in fifty days. Although treatment was regarded as incomplete, he gained 18 pounds (8.2 Kg) and all sinuses had ceased draining and were healing, although the small necrotic ulcerative area persisted in the right axillary region.

Several draining sinuses were reported as still existing on May 5, 1946.

## COMMENT

Treatment with promizole offered little encouragement, because of the variation in therapeutic effects in different cases of the same disease. The lesions of erythema induratum healed in case 3 while the patient was taking the drug, but one year and four months after treatment was stopped the ulcerations recurred in a mild form. In 1 case (not reported in detail) presumptive primary inoculation tuberculosis of the cheek which had been present for three months underwent involution rapidly and did not recur. We have observed previously the phenomena of spontaneous involution in primary inoculation tuberculosis, but the involution was not so rapid as in this case. Results of treatment with promizole in cases of lupus vulgaris and of scrofuloderma were for the most part unsatisfactory. In some cases in which promizole was used in treatment of other types of tuberculosis at the clinic, it produced complications, which on occasion required discontinuing its use. Although leukopenia and generalized toxic erythema were rare in these cases, they were the most serious reactions. Headache and gastric discomfort and nausea were fairly common complications. Although these reactions limited the amount of the drug that could be given and occasionally prevented further administration, no serious sequelae occurred. No doubt the continued use of promizole in the presence of these reactions would have produced serious complications.

Streptomycin seemed to offer more encouragement from the beginning, but its therapeutic effects were of short duration in some of the patients in this series of cases, especially those who received relatively small amounts of the drug. The ulcerations and sinuses of the colligativa and suppurative processes responded most satisfactorily to treatment, and the patients' general condition improved somewhat. The ulcerations and the drainage from the sinuses in case 12 were almost completely healed when the patient left the hospital at the completion of the first course of treatment with 17.6 Gm of streptomycin, only to recur four months later. In 1 case of lupus vulgaris (case 10), the ulceration healed and infiltration was reduced materially, however, biopsy which was performed at the end of the course of treatment revealed active classic tubercle formation. In case 8, in which tuberculosis miliaris disseminata faciei and active pulmonary tuberculosis were present, the pulmonary lesion involuted during treatment. The patient gained 16 pounds (7.3 Kg), but the lesions of the face which improved temporarily, were unchanged after 100 Gm of streptomycin had been given in six months, during which the patient was in bed. Because these patients were in the hospital the general improvement and gain in weight should not be attributed entirely to the streptomycin.

Streptomycin produces few reactions but is more toxic than penicillin. Urticaria, headache and local discomfort at the site of injection were

not troublesome in our cases. Vertigo, in the whole series of cases of tuberculosis of various types treated with streptomycin was a common and troublesome reaction, which persisted for several months after treatment. The impurities encountered in some of the earlier preparations of streptomycin produced reactions of a histamine-like type and toxic erythema, however, these impurities are not present in the more recent preparations.

In 3 cases streptomycin was given after promizole had failed to produce any improvement. As yet we have not used streptomycin and promizole at the same time.

#### CONCLUSIONS

Conclusions are not warranted in an appraisal of promizole and streptomycin in the treatment of cutaneous tuberculosis after such a short experience in a comparatively few cases. We now believe that treatment was inadequate in some of the cases. Because there were no precedents for us to follow in treatment with these drugs, we have felt our way along and have not been without some encouragement. When sufficient quantities of streptomycin are available, we plan to give some patients with cutaneous tuberculosis a minimum of 2 Gm per day for several months. In the series of patients we treated, those who had scrofuloderma and received the larger doses of streptomycin derived the most benefit. It seems probable that the results of treatment of early primary infections, such as inoculation types of tuberculosis of the skin, may be expected to be better than the results of treatment of long-standing organized processes or extensive id reactions in which few tubercle bacilli are present. A therapeutic parallelism in this regard may exist in early and parenchymatous syphilis. We have not overlooked the possibility that in the patients with sinuses and ulcerations the drugs used might have been effective primarily against the secondary bacterial invaders, but this appears improbable because of the limited range of action of these substances and the failure of other antibacterial agents in similar circumstances.

It appears that streptomycin, although not the ideal agent for the treatment of cutaneous tuberculosis and tuberculids, does offer considerable encouragement because of its therapeutic efficacy in guinea pigs inoculated with tuberculosis and because of the varying degrees of improvement in human beings. The therapeutic trials should be continued, and more should be done to stimulate further laboratory investigations for a therapeutic agent that will have a more intense specific action against tubercle bacilli in human beings.

## ELEPHANTIASIS NEUROMATOSA

A Manifestation of von Recklinghausen's Disease

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VON RECKLINGHAUSEN'S disease or multiple neurofibromatosis, is a form of congenital dysplasia manifested by developmental changes in the nervous system, the skin, the bones and the muscle. The disease is frequently familial and may be associated with endocrine imbalance, muscle weakness, or paralysis due to involvement of the cerebrospinal system.

Cutaneous lesions may be divided into three general types: (1) café-au-lait spots associated with freckles or hyperpigmentation, (2) molluscum fibrosum—superficial dermal tumors caused by proliferation of the connective tissue of peripheral nerve sheaths, and (3) subcutaneous neurofibroma, distorting the skin contour.

Nervous involvement is due largely to the dominant tissue of the nerve sheath—neurectodermal Schwannman splanctum.<sup>1</sup> Although there is a controversy as to the origin of the connective tissue, the majority opinion indicates that the Schwann sheath cells are the source of the connective tissue, causing neurofibrotic growths which may involve one nerve, a sheath or a plexus of nerves, or may be generalized to include cranial, spinal and sympathetic nerves. It should be mentioned that there is a tendency to sarcomatous change in the neurofibrotic tumors found in von Recklinghausen's disease.<sup>2</sup> Cumbersome lesions, there-

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1 (a) Masson, P. Histogenèse des neurofibromes cutanés diffus, *Bull. Soc. franç. de dermat. et syph.* **42** 1278, 1935. (b) Masson, P. Tumeurs encapsulées et bénignes des nerfs, *Rev. canad. de biol.* **1** 209, 1942. (c) Masson, P. Recklinghausen's Neurofibromatosis, Sensorv Neuromas and Motor Neuromas, in *Contributions to the Medical Sciences in Honor of Dr. Emmanuel Libman by His Pupils, Friends and Colleagues*, New York, International Press, 1932, vol. 2, p. 739. (d) Stout, A. P. Tumors of Peripheral Nerves, *New England J. Med.* **225** 314, 1941. (e) Murray, H. R., Stout, A. P., and Bradley, C. F. Schwann Cell Versus Fibroblasts as the Origin of the Specific Nerve Sheath Tumor, *Am. J. Path.* **16** 41, 1940. (f) Geschickter, C. F. Tumors of the Peripheral Nerves, *Am. J. Cancer* **25** 377, 1935.

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fore, should have complete excision, for new lesions contiguous with an old lesion, or even in a new location, may undergo sarcomatous change

Skeletal changes frequently associated with von Recklinghausen's disease have been found most commonly to be scoliosis,<sup>3</sup> abnormalities of excess<sup>4</sup> and deficient growth<sup>5</sup> Each of these changes is sometimes seen in the same case Irregularities of outline of the shafts of the long bone, including changes which appear as subperiosteal bone cysts (in reality, neurofibromatosis of the periosteal nerve with outer layer of calcification due to periosteal reaction), represent other changes in the skeletal system which are sometimes associated with this disease<sup>6</sup> All the bone changes observed could be explained on the basis of tumor tissue characteristic of neurofibroma involving the bone by involvement of the periosteal nerve, the lymphatics and the epiphyseal cartilage Neurofibromatous involvement of the marrow cavity has been recorded<sup>7</sup>

Endocrine changes sometimes associated with multiple neurofibromatosis are menstrual abnormalities, acromegaly, cretinism, delayed or incomplete sexual development, myxedema, tetany, Addison's disease

2 (a) Geschickter<sup>1c</sup> (b) Lewis, D, and Hart, D Tumors of Peripheral Nerves, *Ann Surg* **92** 961, 1930 (c) Charache, H Multiple Neurofibroma with Sarcomatous Transformation and Skeletal Involvement, *Arch Dermat & Syph* **40** 185 (Aug) 1939 (d) Miller, A Neurofibromatosis with Reference to Skeletal Changes, Compression Myelitis and Malignant Degeneration, *Arch Surg* **32** 109 (Jan) 1936 (e) Lewis, D Elephantiasis Nervorum, *Ann Surg* **93** 209, 1931

3 (a) Miller<sup>2d</sup> (b) Brooks, B, and Lehman, E P Bone Changes in Recklinghausen's Neurofibromatosis, *Surg, Gynec & Obst* **38** 587, 1924 (c) Lehman, E P Recklinghausen's Neurofibromatosis and the Skeleton A Plea for Complete Study of Disease, *Arch Dermat & Syph* **14** 178 (Aug) 1926 (d) Gould, E P The Bone Changes Occurring in von Recklinghausen's Disease, *Quart J Med* **11** 221, 1918 (e) Stalman, A Nerven- Haut- und Knochenveränderungen bei der Neurofibromatosis Recklinghausen und ihre entstehungsgeschichtlichen Zusammenhänge, *Virchows Arch f path Anat* **289** 96, 1933 (f) Diasio, F A Elephantiasis Neuromatosa (von Recklinghausen's Disease), *Urol & Cutan Rev* **36** 104, 1932 (g) Brunner, W Beitrag zur Elephantiasis neuromatodes, *Deutsche Ztschr f Chir* **246** 751, 1936 (h) Heusch, K Ueber die Beziehungen des Sympathicus zur Neurofibromatose und dem partiellen Riesenvuchs, *Virchows Arch f path Anat* **255** 71, 1925 (i) Jordan, M Pathologisch-anatomische Beiträge zur Elephantiasis congenita, *Beitr z path Anat u z allg Path* **8** 71, 1890

4 (a) Stalman<sup>3e</sup> (b) Brunner<sup>3g</sup> (c) Heusch<sup>3h</sup> (d) Jordan<sup>3i</sup> (e) Spittel, R L, and Fernando, S E Elephantiasis Neuromatosa, *Brit M J* **1** 596, 1929

5 Brooks<sup>3b</sup> Stalman<sup>3e</sup> Heusch<sup>3h</sup> Jordan<sup>3i</sup>

6 Brooks<sup>3b</sup> Stalman<sup>3e</sup> Spittel and Fernando<sup>4e</sup>

7 Friedman M M Neurofibromatosis of Bone, *Am J Roentgenol* **51** 623, 1944

and a diabetic blood sugar curve.<sup>8</sup> Thus, multiple neurofibromatosis may manifest itself in many ways. One of the rarer and more interesting types seen in conjunction with von Recklinghausen's disease is that of elephantiasis neuromatosa of Virchow—a fibromatosis of cutaneous nerves, merging into a diffuse overgrowth of subcutaneous tissue and skin, giving an elephantiasis, or enlargement, of the part affected.<sup>9</sup> The overlying skin may be normal but frequently is thickened and pigmented. At times, thickened or coiled nerves may be palpated within. Such an enlargement often appears in childhood.<sup>10</sup> It is usually progressive and disfiguring and is sometimes incapacitating and painful. The frequently associated familial tendency and bone and endocrine changes are also seen with this variation.<sup>11</sup> Of course, in multiple neurofibromatosis there may be any gradation of tumor, varying from the small cutaneous elevations to the huge tumors involving an entire lower extremity, causing extreme deformity and showing many associated bone changes. The dividing or differentiating line between neurofibromatosis, plexiform neurofibroma and elephantiasis neuromatosa is difficult to determine. Our 2 cases represent the large lesions of the elephantiasis neuromatosa group.

The typical history is that of a child (one of whose parents had a history of von Recklinghausen's disease) presenting signs of generalized neurofibromatosis which has slowly progressed from a small skin nodule into a mass. This mass is most frequently located around the neck or on the extremities.<sup>12</sup> In 8 of the 42 cases reported by Bruns,<sup>13</sup> a mass developed in the neck.

8 (a) Charache<sup>2c</sup> (b) Brunner<sup>3c</sup> (c) Rosenthal, D. B., and Willis, R. A. The Association of Chromaffin Tumors with Neurofibromatosis. *J. Path. & Bact.* **42**:599, 1936. (d) Tucker, B. R. Von Recklinghausen's Disease with Especial Consideration of Endocrine Connection, *Arch. Neurol. & Psychiat.* **11**:308 (March) 1924. (e) Levin, O. L. Von Recklinghausen's Disease. Its Relation to the Endocrine System, *Arch. Dermat. & Syph.* **4**:303 (Sept.) 1921. (f) Louste, Caillaud, and Darquier. Syndrome de Recklinghausen et acromégalie. *Publ. Soc. franç. de dermat. et syph.* **33**:54, 1925.

9 Virchow, R. Die krankhaften Geschwulste, Berlin, A. Hirschwald, 1863, vol. 1, cited by Jordan.<sup>31</sup>

10 (a) Brooks<sup>3b</sup> (b) Heusch<sup>3h</sup> (c) Jordan<sup>31</sup> (d) Spittel and Fernando<sup>4c</sup> (e) Corsi, H. Rare Type of von Recklinghausen's Disease. *Proc. Roy. Soc. Med.* **25**:1739, 1932.

11 (a) Diasio<sup>3f</sup> (b) Heusch<sup>3h</sup> (c) Jordan<sup>31</sup> (d) Spittel and Fernando<sup>4c</sup> (e) Anzinger, F. P. Congenital Plexiform Neurofibromas and Elephantiasis Neuromatosa of Right Arm and Neck (von Recklinghausen's Disease). Supplementary Report, *J. A. M. A.* **96**:1381 (April 25) 1931.

12 (a) Diasio<sup>3f</sup> (b) Brunner<sup>3c</sup> (c) Heusch<sup>3h</sup> (d) Jordan<sup>31</sup> (e) Spittel and Fernando<sup>4c</sup> (f) Corsi<sup>10e</sup> (g) Anzinger<sup>11e</sup> (h) Härtel, F. Fall von risen-

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The common signs and symptoms are pain and/or the presence of a deforming, incapacitating mass. Bone and endocrine changes frequently occur, possibly because of the widespread and extensive form of multiple neurofibromas present.

Evaluation and treatment consist of a complete skeletal roentgenologic examination, an endocrine study (including a study of blood sugar, alkaline and acid phosphatase, chlorides, etc.), followed, if possible, by extensive removal of the affected part, as these lesions tend toward



Fig 1 (case 1)—*A*, note lobulated mass hanging from the neck down over the wall of the chest. *B*, clinical photograph taken four and one-half years after the operation.

sarcomatous change and recurrence.<sup>14</sup> In 1 case cited in the literature a sarcoma developed in the region of the breast three years after removal of an elephantiasis lesion of the arm.<sup>12h</sup>

The following 2 cases were seen at the Ellis Fischel State Cancer Hospital.

hafter Lappenelephantiasis bei einer Japanerin, *Deutsche Ztschr f Chir* 208 423, 1928

13 Bruns, P. Ueber das Rankenneurom, *Beitr z klin Chir* 8 1, 1891

14 Brunner<sup>2g</sup> Hartel<sup>12h</sup>

## REPORT OF CASES

CASE 1—G E, a 40 year old man, entered the hospital on Feb 7, 1941, complaining of redundant, nonpainful tumors of the neck, the chest and the scalp since birth. The tumors had grown with a rate corresponding to the patient's growth. Approximately three years before the patient's admission the tumors began to grow more rapidly. The patient's mother had von Recklinghausen's disease.

Physical examination showed a soft, pedunculated, freely movable mass 8 cm in diameter on the left side of the neck, beginning at the upper part of the nucha and extending down to the level of the fourth cervical vertebra. There was a redundant soft pedunculated mass, apparently arising from subcutaneous tissue extending from the left mastoid process along the left mandible to the left nipple.



Fig 2 (case 1) —Roentgenologic view of the cervical spine showing excessive deformity.

(fig 1 A) This was covered with brown, atrophic, excoriated, reddened skin. There were several areas over 1 cm in diameter on the skin of the wall of the chest which had the typical cafe-au-lait appearance. In addition to the primary lesion, this patient had several congenital anomalies. There was a severe deformity of the cervical vertebrae with posterior bowing and fusion, the left clavicle was bowed anteriorly with overriding of the opposite pieces, and the left leg was bowed anteriorly and laterally, with flattening of the tibia in the anterior-posterior diameter. This deformity had been present since birth. Examination of the skin over the rest of the body revealed several cafe-au-lait spots and molluscum fibrosum on the thorax and the abdomen. Over the left rectus muscle there was a tumor measuring 2 cm which was similar in consistency to the large one.

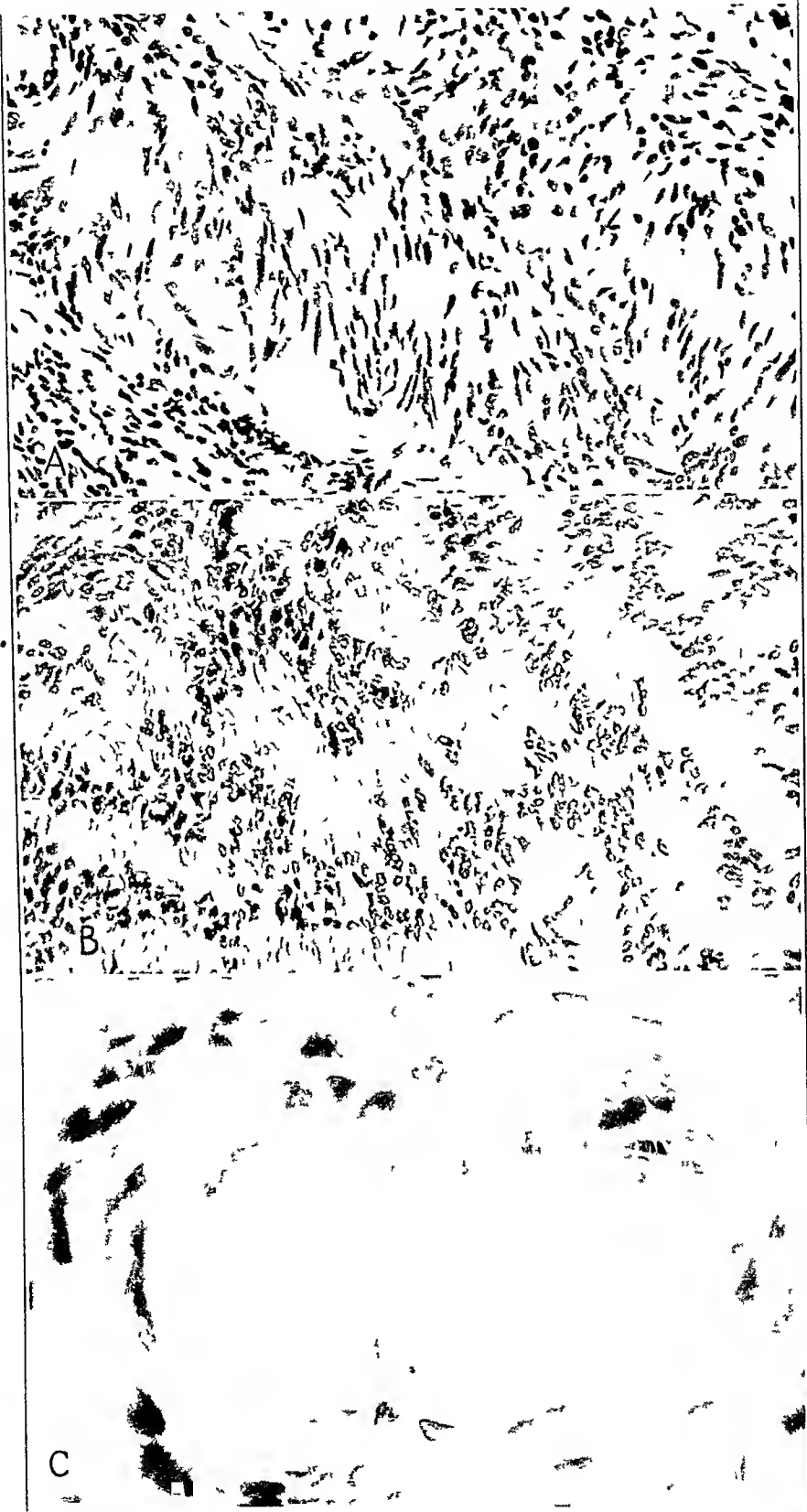


Figure 3  
(See legends on opposite page)

previously described. There was also a tumor 0.5 cm. in diameter over the right scapula.

Roentgenograms revealed a multiple soft tissue thickening of the chest, the left shoulder girdle and the supraclavicular and infraclavicular regions, asymmetry of the rib cage, deformity of the cervical column with associated arthritic changes, underdevelopment of the first and second cervical vertebrae, developmental changes of the left clavicle, apparently secondary to the tumors of the left shoulder girdle and developmental deformity of both bones of the left leg. Blood count and urinalysis were within normal limits. A serologic test for syphilis elicited a negative reaction.

It was decided that this lesion could best be treated by a two stage excision. The mass in the neck and in the wall of the chest was excised on February 12, and a split thickness graft was applied. Twenty days later the mass in the scalp and the neck was excised and the tumor was found to extend to the foramen magnum. A scar subsequently developed in the midline of the neck, but this was corrected with a plastic procedure. There was no evidence of recurrence one and a half years after this treatment.

*Pathologic Examination*—The surface of the specimen had an elephant hide appearance, and in a few areas the skin was thrown into folds and wrinkles. On cut section the tumor was gray-white. It cut with difficulty and was homogeneous throughout; with no areas of hemorrhage or necrosis. Microscopically, the sections showed areas characteristic of the loose-textured arrangement of Schwannian cells. In other zones cells had more deeply stained nuclei and tended to be larger and somewhat irregular. The tumor invaded the muscle, separating its bundles. There were areas where the arrangement of cells suggested strongly the histologic pattern which one sees in neurilemmoma (fig. 3 A and B). There were also structures which caricatured the Wagner-Meissner tactile corpuscles (fig. 3 C). A questionable pacman body was observed.

*Microscopic Diagnosis*—The diagnosis on the basis of microscopic examination was elephantiasis neuromatosa.

The clinical course and pathologic picture were typical of elephantiasis neuromatosa, a manifestation of von Recklinghausen's disease. The associated congenital bony deformities were those occasionally seen in this disease.

CASE 2—O. B., a 22 year old man, entered the hospital Nov. 15, 1940, with the chief complaint of soft masses under the right arm and under the right pectoral region which had been present for ten years. These small, soft masses grew progressively larger but caused no pain. A biopsy was performed four years previous to his admission, and soon afterward pain appeared in the right arm.

Physical examination revealed a lobulated, pedunculated, movable mass, the base of which was attached to the right pectoral region of the chest wall (fig. 4).

#### EXPLANATION OF PLATE

Fig. 3 (case 1)—A, photomicrograph of an area in the tumor showing resemblance to the neurilemmoma in B. B, photomicrograph of a typical neurilemmoma with palisading and characteristic arrangement. Moderate enlargement. C, photomicrograph (high power) of a structure resembling a Wagner-Meissner tactile corpuscle.

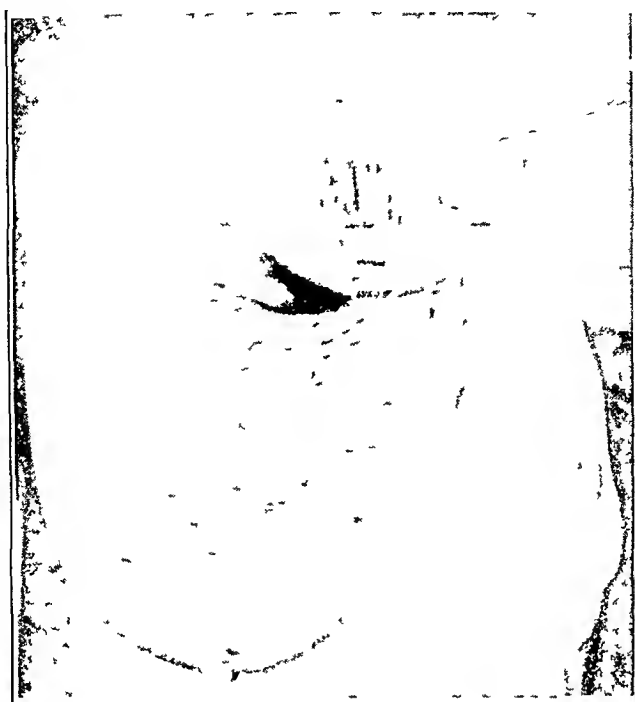


Fig 4 (case 2)—Clinical photograph of soft pendulous mass in the axilla. Note pigmentation of the tumor and the cafe-au-lait spot near the nipple.



Fig 5 (case 2)—Gross photograph of large nodular tumor mass with wrinkled skin. The finger-like processes close to the ruler represent the tumor which extended between the ribs.

The underlying skin was gray-white and nodular to palpation. There were multiple areas of light brown pigmentation scattered over the skin of the arms.

The clinical diagnosis was elephantiasis neuromatosa.

On November 20 an excision of the lesion was performed. At the time of operation it was found that the lesion extended into the uppermost part of the axilla and had digitations extending between the ribs in the third and fourth interspaces, where it appeared to arise from the intercostal nerves and extend back to the vertebral column posteriorly. The fourth rib was so extensively surrounded that it had to be resected. A radical axillary dissection was also performed. The large resultant defect was covered with split thickness graft from the thigh. The operative course was uneventful, and a postoperative roentgenologic examination revealed minimal curvature of the dorsal vertebral column, with convexity to the right. There was slight increase in density of the vertebrae, hypertrophic arthritis and a minimal amount of demineralization of the bone. Subsequent clinical visits and follow-up revealed no new enlargement of any of the remaining neurofibromas, and four and a half years after operation there was no evidence of disability or of recurrence.

*Pathologic Examination*—Examination of the specimen revealed firm poorly defined nodularities palpable underneath the skin. Cut sections showed nodular gray-white, firm tissue with multiple areas of necrosis. There were finger-tip-like processes which were identified as portions of the tumor which penetrated the costal interspaces. The rib was not grossly or microscopically invaded by the tumor (fig 5). Microscopically, the changes in this tumor were identical with those found in the previous case.

This case of elephantiasis neuromatosa extensively involved the chest wall and the axilla. It closely resembled the case of Pomorski cited by Bruns,<sup>13</sup> in which the tumor arose from intercostal nerves and extended into the pleural cavity. It is unfortunate that no preoperative roentgenograms were taken, for they might have given indirect evidence of growth of the tumor between the ribs.

#### SUMMARY

Two patients with typical, rather extensive elephantiasis neuromatosa with secondary bone changes were treated by radical surgical intervention.

# DYSKERATOSIS CONGENITA WITH PIGMENTATION, DYSTROPHIA UNGUIUM AND LEUKOPLAKIA ORIS

Patient with Evidence Suggestive of Addison's Disease

JOHN GARB, M.D.

NEW YORK

IN A PREVIOUS article<sup>1</sup> 2 brothers were described who had the main features of the syndrome named by Cole and associates. Of considerable importance was the pronounced improvement in the leukokeratotic patches of the mucous membrane of the mouth and tongue of the older brother, J. W., following medication for several weeks with testosterone propionate. In this paper I am reporting the findings in the patient J. W. of the various tests and examinations and the results of treatments with adrenocortical hormones, all of which are suggestive of the presence of associated Addison's disease. This is a part of the investigative work now being carried on by Dr. Fred Wise and myself, with the view of collecting data on the presence of pathologic changes in the adrenal glands in various chronic and resistant dermatologic diseases, as has already been reported by Garb and Wise in a case of mycosis fungoides with bullous lesions.<sup>2</sup> The following description is a brief report of the 2 brothers.

## REPORT OF A CASE

J. W., an American-born Jew, had hyperpigmented and depigmented patches on the trunk and extremities. The patches were arrayed in a fine network enclosing normal areas of skin. The skin was dry. The finger nails and toe nails were dystrophic, the finger nails being either wanting or reduced to thin remnants. There were leukokeratotic patches on the buccal mucosa on the left side and on the dorsal surface of the tongue. The teeth were decayed, and many were missing. He had ulcerations in the commissures of the lips. There was an

From the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, Columbia University College of Physicians and Surgeons, service of Dr. Fred Wise.

1 Garb, J., and Rubin, G. Dyskeratosis Congenita with Pigmentation, Dystrophia Unguium and Leukoplakia Oris (Cole and Others). Report of the Cases of Two Brothers, with Improvement in the Leukoplakic Patches in One with Androgenic Medication, *Arch. Dermat. & Syph.* **50**: 191 (Sept.) 1944.

2 (a) Garb, J., and Wise, F. Mycosis Fungoides with Bullous Lesions. Report of a Case Resistant to Roentgen and Arsenical Therapy, Effects of Empiric Therapy, Partly Based on Laboratory Investigations, *Arch. Dermat. & Syph.* **48**: 359 (Oct.) 1943. (b) Garb, J. Mycosis Fungoides with Bullous Lesions. Special Tests and Laboratory Data Indicating Adrenal Insufficiency, *ibid.* **49**: 315 (May) 1944.

associated atrophy of the dorsal surfaces of the hands, resembling acrodermatitis chromica atrophicans. The patient was mentally retarded, underweight and physically weak. There was tearing of the eyes due to closure of the tear ducts. On the skin about the nails and on the extremities he had recurrent infections, which were slow to heal.

The younger brother showed similar anomalies except that they developed later in life and were of a milder form.

Routine and special laboratory tests<sup>1</sup> were performed, which have no particular significance for the subject herein discussed except the hemogram taken on Feb 2, 1943, which is here again recorded. It showed 11.5 Gm of hemoglobin per hundred cubic centimeters of blood and 3,480,000 erythrocytes and 6,400 leukocytes per cubic millimeter. The differential count showed 39 polymorphonuclear neutrophils, 2 eosinophils, 8 monocytes, 40 lymphocytes and 11 band neutrophils per hundred cells.

Other laboratory data not previously reported are as follows. The color index on Feb 2, 1943 was 1.2 (normal 0.9 to 1.0) and the volume index 1.7 (normal 0.85 to 1.15). On April 27, 1943 the hemogram showed 50 polymorphonuclear

TABLE 1—*Chemical Observation on the Blood*

Date	Specimen Examined	Constituents (Normal Range in Parentheses)	Amount, per 100 Cc
2/25/43	Serum	Proteins	
		Total (6 to 8 Gm)	5.0 Gm
		Albumin (4 to 5 Gm)	3.7 Gm
		Globulin (2 to 3 Gm)	1.3 Gm
		Ratio (1.6 to 2.1)	2.6:1%
2/25/43	Whole blood	Ratio of urea nitrogen to non protein nitrogen (35:45)	46%
2/25/43	Serum	Phosphates, inorganic (adults 3.5 to 4.0)	3.4 mg
3/19/43	Serum	Phosphatase activity (alkaline) (3 to 5)	2.6 (Bodansky units)
2/25/43	Serum	Calcium	
		Total (9.6 to 11)	11.4 mg
2/25/43	Serum	Ionized (4.8 to 6.3)	6.1 mg
2/25/43	Serum	Cholesterol (160 to 230) (lipid partition otherwise normal)	270.0 mg

leukocytes, 42 lymphocytes and 8 monocytes. On Jan 11, 1944 the erythrocyte count was 3,500,000, hemoglobin content, 11.5 Gm (80.7 per cent), and leukocyte count, 7,350, with 27 polymorphonuclear neutrophils, 57 lymphocytes and 13 band neutrophils. The color index was 0.98 and the volume index 1.2. The sedimentation rate was 20 mm per hour (maximum in men 10 mm per hour, by the Westergren method). The dextrose tolerance test gave a flattened curve. The blood sugar on a fasting stomach was 65 mg. After the ingestion of 100 Gm of dextrose, the half hour and five hourly samples contained respectively 85, 80, 60, 65, 65 and 55 mg per hundred cubic centimeters of whole blood. The urine did not contain sugar. The results of the determination of blood volume for plasma and whole blood were within normal limits. The plasma volume was 49 cc per kilogram (normal 49 to 55) and the whole blood 90 cc per kilogram (normal 72 to 100). The viscosity of the whole blood was 7.4 units (normal 4.4 to 5.5).

Two biopsy specimens from a hyperpigmented area showed poikiloderma-like changes. A biopsy specimen of the lesion of the mouth showed leukoplakia.

Laboratory data are given in the tables to facilitate reading and interpretation.

The patient was hospitalized at the New York Post-Graduate Hospital from March 17 to March 24, 1943 for the purpose of having the Robinson, Power and Kepler<sup>3</sup> procedures performed and other special tests done which were needed to furnish additional evidence of possible deficiency or malfunction in the secretions of the adrenal gland as suggested by the clinical signs and symptoms

TABLE 2—*Determination of Vitamin C Content in the Blood and Urine*

Date	Specimen Examined	Constituents	Amount, per 100 Cc
3/19/43	Blood plasma	Vitamin C (0.7 to 1.4 mg)	0.8 mg
3/23/43	Blood plasma	Vitamin C (0.7 to 1.4 mg)	0.7 mg
6/17/43	Blood plasma	Vitamin C (0.7 to 1.4 mg)	0.4 mg
6/17/43	Urine	Vitamin C saturation test (urine excretion after injection of 1 Gm of vitamin C intravenously)	
		1½ hr	211 mg per 210 cc
		3½ hr	138 mg per 150 cc
		5 hr (over 450 mg)	349 mg per 360 cc
		Saturation index (over 500)	429 mg in 24 hr

*Robinson, Power and Kepler Tests*—The urine voided at 10 30 p m on March 25, 1943, was discarded. The urine voided later, up to and including 7 30 a m, measured 219 cc, and the largest specimen of urine voided during the day yielded 217 cc. Chemical examination revealed 960 mg of chlorides and 1,022 mg of urea nitrogen in the urine and 595 mg of chlorides and 17 mg

TABLE 3—*Special Chemical Observations on the Urine*

Date	Specimen Examined	Constituents	Amounts, per 100 Cc	Amounts, per Volume
3/19/43	Urine	Creatinine and creatine	0.30 Gm	1.93 Gm
		Creatinine	0.26 Gm	1.67 Gm
		Creatine	0.04 Gm	0.26 Gm
3/19/43	Urine	17 ketosteroids (8 to 23 mg) (in 643 cc of urine voided in 24 hr)	6.5 mg	
		(in 1 160 cc of urine voided in 24 hr)		

of urea nitrogen in the blood plasma. By substitution of these figures in the following formula, which is used for Addison's disease

$$A = \frac{\text{Urea in urine (mg/100 cc)}}{\text{Urea in plasma (mg/100 cc)}} \times \frac{\text{Chloride in plasma (mg/100 cc)}}{\text{Chloride in urine (mg/100 cc)}} \times \frac{\text{Volume of day urine (cc)}}{\text{Volume of night urine (cc)}}$$

the equation figure of 36.9 is obtained, the significance of which is discussed later.

The daily temperature in the hospital per os ranged from normal to 96.5 F.

Scout films of the abdomen for possible changes in the suprarenal region, taken by Dr. William H. Meyer, "showed no abnormality of the denser organs. The left kidney appeared a shade larger than the right. They were otherwise of normal contour and illumination. There were no abnormal calcifications."

*Fractional Gastric Analysis* (Jan 26, 1944)—A fasting specimen was first taken. A pint (0.5 liter) of thin gruel was then given, and specimens were

3. Robinson, F. J., Power, M. H., and Kepler, E. J. Two New Procedures to Assist in Recognition and Exclusion of Addison's Disease, Proc. Staff Meet., Mayo Clin 16:577 (Sept 10) 1941.

obtained twenty and forty minutes later. Histamine phosphate, 0.5 cc of 1 to 1,000 solution, was then injected subcutaneously, and samples were collected at the end of twenty and forty minutes. Results obtained are given in table 4.

Determination of blood pressure was taken on several occasions with the patient in the recumbent and upright positions, with results given in table 5.

*Follow-up of the Patient J W Since March 1944*—The patient continued to take dried yeast in tablespoon doses three times a day after meals for eight

TABLE 4—Results of Fractional Gastric Analysis

Specimen	Milliequivalents of Cl per Liter		Color	Mucus	Lactic Acid
	Free HCl,	Total Acidity			
Fasting	Negative	29	Gray white	Mucoid	Negative
one pint (0.5 liter) thin gruel taken					
20 min after	Negative	10	Gray white	Fluid	Negative
40 min after	Negative	10	Gray white	Fluid	Negative
Histamine phosphate injected					
20 min after	Faint trace	18	Gray white	Fluid	Negative
40 min after	20 degrees	49	Gray white	Fluid	Negative

months, thus sufficient time was allowed for any definite manifestation of regression of the leukoplakic patches that might result from the ingestion of such large doses of vitamin B complex.<sup>4</sup> There was, however, no noticeable change during this prolonged period of trial in the lesions, which had partly recurred following the discontinuance of the use of the androgenic medicament in December 1943.<sup>5</sup> On Jan 18, 1945 oral administration of adrenal cortical extract<sup>6</sup> was prescribed instead of the dried yeast, 1 tablet to be taken three

TABLE 5—Rowntree or Schellong Tests<sup>14</sup>

Date	Right Arm		Left Arm	
	Horizontal Position	Upright Position	Horizontal Position	Upright Position
1/1/48	120/60	110/60	120/60	110/60
1/22/44	100/20	110/60	100/20	110/60
1/25/44	100/40	110/50	105/50	120/60
1/18/45	100/60	100/40	100/60	110/60
4/12/45	100/50	120/60	110/70	120/60

times a day before meals. After six weeks 2 tablets of adrenal cortical extract were given three times a day. Photographs were taken on Jan 18 and on April 26, 1945. During these three months the patient gained only 1 Kg. in

4 Martin, H., and Koop, E. C. The Precancerous Mouth Lesions of Avitaminosis B, *Am J Surg* **57** 207 (Aug.) 1942.

5 Garb and Rubin,<sup>1</sup> p. 195.

6 The adrenal cortical extract was Cortalex, The Upjohn Company, Kalamazoo, Mich. Each tablet presents the physiologically active adrenal cortical hormone contained in 5 Gm of fresh adrenal gland, together with 15 mg of ascorbic acid.

weight He stated, however, that he felt more vigorous He did not tire so easily as formerly His appetite was still poor, but it was improving There was a good change in the blood pressure readings (table 5) The leukoplakic patches showed definite signs of regression on the middle and lower borders of the left cheek

## COMMENT

*Interpretation of Laboratory Data*—The hemograms showed an increase in the band neutrophils, or stab cells of Schilling, which are immature or nonsegmented cells This is a shift to the left occurring in chronic infections<sup>7</sup> The increased sedimentation rate of 20 mm per hour is likewise indicative of a chronic infection<sup>8</sup> The total protein content in the blood serum of only 5 Gm (table 1) corresponds with its diminution in malnutrition<sup>9</sup> The rise in the blood cholesterol level to 270 mg per hundred cubic centimeters was anticipated, as hypercholesteremia occurs among other diseases in various degenerative conditions<sup>10</sup>, so was the increase in the twenty-four hour urinary excretion of creatinine to 1.67 Gm (normal, 1.25 Gm), as shown in table 3, expected, as larger amounts of creatinine are eliminated in the urine in wasting diseases because of tissue catabolism<sup>11</sup>

*Evidence Suggestive of Adrenal Insufficiency*—The following evidence is indicative of hypofunction of the adrenals notwithstanding the normal endocrinologic findings<sup>1</sup> and the high equation figure of 36.9, which according to Robinson and colleagues<sup>12</sup> would be interpreted as indication against the presence of Addison's disease

1 The patient had complaints of asthenia, loss of weight, chronic constipation, depression of the sexual function and glossitis

2 There were gastrointestinal symptoms manifested by attacks of vomiting, which were at times severe and accompanied with the presence of blood in the vomitus Gastrointestinal disturbances occur sometimes in Addison's disease and when severe may simulate a gastric crisis<sup>13</sup>

3 The Rowntree or Schellong test<sup>14</sup> (table 5) elicited a positive reaction The blood pressure readings on Jan 1, 1943 were lower by 10 degrees in both arms in the upright position as compared with those

7 Kolmer, J. A. *Clinical Diagnosis by Laboratory Examination*, New York, D. Appleton-Century Company, Inc., 1943, p. 30

8 Kolmer,<sup>7</sup> p. 21

9 Kracke, R. R., and Parker, F. P. *A Textbook of Clinical Pathology*, Baltimore, Williams & Wilkins Company, 1940, p. 317

10 Kracke and Parker,<sup>9</sup> p. 294

11 Kolmer,<sup>7</sup> p. 73

12 Robinson, Power and Kepler,<sup>3</sup> p. 580

13 Harrop, G. A. *The Adrenal Glands*, in Tice, F. *Practice of Medicine*, Hagerstown, Md., W. F. Prior Company, Inc., 1921, vol. 8, p. 322

14 Wolf, W. *Endocrinology in Modern Practice*, ed. 2, Philadelphia, W. B. Saunders Company, 1939, p. 937

in the horizontal posture. On Jan 22 and 25, 1944 the readings were higher in both arms in the upright position. This improvement and the fact that the patient felt generally better and stronger should justifiably be attributed to the use of testosterone propionate.

4 There was pigmentation, which was generalized, more pronounced and deepest in the areas exposed to light, as the face and neck, with the bathing trunk area unaffected, and there were numerous vitiliginous patches on the face, neck and trunk, which are commonly seen in Addison's disease<sup>15</sup>

5 Results of examination of the creatine and creatinine content in the urine were indicative of renal insufficiency. The combined creatine and creatinine value was 0.30 Gm., and the creatine content was 0.04 Gm., or 13.3 per cent, in a twenty-four hour volume of urine (table 3). This, according to Stemach and his co-workers,<sup>16</sup> points to a deficiency in the secretion of androgens, as such a hormonal deficiency is present if the amount of creatine in the urine is 10 per cent or more of the combined value of the creatine and creatinine. This is corroborated by the low 17-ketosteroid content of 6.5 mg (table 3). Since this hormone is in males an index of the combined activity of the adrenals and the gonads, the low 17-ketosteroid content could reasonably be attributed to deficiency in both these ductless glands.

6 A vitamin C deficiency was present (June 17, 1943, table 2). This may indicate a depletion of vitamin C in the adrenal cortex, since the proper function of this gland depends on the large amount of ascorbic acid<sup>17</sup> which it normally stores.

7 The flat sugar tolerance curve indicated renal insufficiency. Eppinger and Rudinger<sup>18</sup> have shown that patients with Addison's disease (hypoadrenalism) have an increased tolerance for sugar.

8 There was a rise in viscosity of the whole blood to 7.4 units. This is increased in Addison's disease due to anhydremia.

9 Examination of the gastric content showed achlorhydria even after the test meal and yielded only a trace of hydrochloric acid twenty minutes after stimulation with histamine (table 4). A low gastric acidity or complete anacidity is commonly found in Addison's disease.<sup>19</sup>

<sup>15</sup> Harrop,<sup>13</sup> p. 320.

<sup>16</sup> Stemach, E., Kun, H., and Peczenik, O. Diagnostischer Test für hormonbedingte Störungen der männlichen Sexualfunktion und seine klinische Anwendung, *Wien klin Wchnschr* 49:388, 1936, cited by Feldman, S., Pollock, J., and Abarbanel, A. R. Treatment of Senile Pruritus with Androgens and Estrogens, *Arch Dermat & Syph* 46:113 (July) 1942.

<sup>17</sup> Harrop,<sup>13</sup> p. 307.

<sup>18</sup> Eppinger, H., and Rudinger, K., cited by Falta, W. *Erkrankungen der Blutdrüsen*, Berlin, Julius Springer, 1913, p. 276.

<sup>19</sup> Harrop,<sup>13</sup> p. 322.

10 The results of the hemograms indicated adrenal insufficiency Kracke and Parker<sup>20</sup> stated that the blood in Addison's disease is usually normal but that a macrocytic anemia may occasionally be present. The hemograms had the features of moderate macrocytic anemia. This is shown by the lowered erythrocyte count of 3,500,000, the hemoglobin content of 11.5 Gm, the relative lymphocytosis (27 polymorphonuclear neutrophils and 57 lymphocytes) with 13 band neutrophils, the color index of 1.2 and the volume index, which was 1.7 on Feb. 23, 1943 and 1.2 on Jan. 11, 1944.

11 There was an increased urinary excretion of creatine, which occurs in wasting conditions and disorders of the muscles and is present in Addison's disease when the "adynamia is severe."<sup>19</sup> Creatine is not normally found in the urine of normal men, as it is converted into creatinine before excretion, but it may occur in them in amounts up to 196 mg. per twenty-four hours.<sup>11</sup> The patient had the high creatine excretion of 1.93 Gm. per twenty-four hours, or 0.04 Gm. per hundred cubic centimeters of urine.

12 There was response to therapy, as shown by the regression of the bullae of the mouth within three weeks after the administration of testosterone propionate. This may justifiably be attributed to the direct beneficial action of the androgens on the kidneys and adrenal glands similar to the action of the adrenocortical hormones on the latter in Addison's disease.<sup>21</sup>

13 The partial recurrence of the leukoplakic patches within three months following the discontinuance of administration of testosterone propionate,<sup>5</sup> the improvement in the general well-being of the patient, the change for the better in the blood pressure readings of April 12 over those of Feb. 1, 1945 (table 5) and the regression of the leukoplakic patches in the center and lower borders of the oral mucosa following four months of medication with adrenal cortical extract add still further valuable evidence of cortical disturbance.

The low 17-ketosteroid content, the increase in viscosity, the vitamin C deficiency and the good response to testosterone propionate and adrenal cortical extracts point to disease of the adrenal cortex, while the hypotension, the pigmentation and possibly the flat sugar tolerance curve suggest coincident disorder of the adrenal medulla.<sup>22</sup> Since there is an interrelationship between the adrenals and the other ductless glands, especially the anterior pituitary, the relatively small sella turcica, 15 per cent undersize, may be of some significance.

20 Kracke and Parker,<sup>9</sup> p. 684.

21 Selye, H. The Effect of Testosterone on the Kidney, *J. Urol.* **42**: 637 (Oct.) 1939, cited by Garb and Wise,<sup>2a</sup> p. 367.

22 Harrop,<sup>13</sup> p. 308.

There is naturally no way of determining whether the possible derangement of the adrenal glands is a concomitant primary disturbance associated with the syndrome of dyskeratosis congenita with pigmentation, dystrophia unguium and leukoplakia oris, with the resultant sequelae of malnutrition and chronic infection, or whether they are secondarily affected as a sequel of the chronic infection and malnutrition. Sarason<sup>23</sup> proved by autopsy findings that distinct morphologic changes occur in the cortex of the adrenal gland in patients who have suffered from malnutrition, hypertension and inflammatory diseases.

It is interesting to note that Wile,<sup>24</sup> in the discussion of Engman's patient, thought of the possibility of the presence of some malignant change, such as an abdominal neoplasm involving the kidney and suprarenal gland.

#### SUMMARY

I have summarized the laboratory data and special examinations which were performed and have interpreted the results of the treatments given to 1 of 2 brothers with the syndrome of dyskeratosis congenita with pigmentation, dystrophia unguium and leukoplakia oris for the purpose of ascertaining the possible presence of Addison's disease, which was suggested by the symptoms and physical signs.

There was an increase in the band neutrophils, a rise in sedimentation rate, hypoproteinemia, hypercholesteremia and an increased urinary excretion of creatine. These correspond with the expected findings in the patient who had a chronic infection and was suffering from malnutrition and a wasting disease.

The presence of dysfunction of the adrenal glands (hypoadrenalism) is suggested by symptoms of asthenia, loss of weight, positive results from Rowntree or Schellong tests, cutaneous pigmentation, which is deepest in the areas exposed to light, tests indicating androgen deficiency, vitamin C deficiency, flat sugar tolerance curve, increased viscosity of the blood, relative achlorhydria, increased urinary excretion of creatine, the good response of the leukokeratotic patches to testosterone propionate, which is similar in its beneficial action on the adrenal glands to the hormones of the adrenal cortex, the improvement in the mental and physical condition of the patient, and the partial regression of the leukoplakic patches of the oral mucosa following oral therapy with adrenal cortical extract. This hypoadrenia either may be associated with the syndrome of dyskeratosis congenita with pigmentation, dystrophia unguium

23 Sarason, E. L. Adrenal Cortex in Systemic Disease, *Arch. Int. Med.* **71**:708 (May) 1943.

24 Wile, U. J., in discussion on Engman, M. A Unique Case of Reticular Pigmentation of the Skin with Atrophy, *Arch. Dermat. & Syph.* **13**:686 (May) 1926.

and leukoplakia oris or represent a secondary effect of the chronic infection and malnutrition

This contribution presents another chronic disease of the skin with suggestive clinical and laboratory evidence of pathologic alterations in the adrenal glands which has previously been reported in a case of mycosis fungoides with bullous lesions<sup>2</sup>

219 East Nineteenth Street

# PRIMARY LICHEN AMYLOIDOSIS

## Report of Necropsy

SIGMUND S GREENBAUM, M D

AND

JOHN T BAUER, M D \*

PHILADELPHIA

**D**EPOSITS of amyloid in the skin associated with widespread systemic deposits have become more generally recognized recently. Primary amyloidosis of the skin must be exceedingly uncommon, however, the first report in the American literature appearing in 1931.<sup>1</sup> This was based on European, not American, cases. For the condition to be considered primary, there should be no evidence of deposits of amyloid in the viscera. This can be ascertained after complete post-mortem examination, hence any such diagnosis during life cannot be more than presumptive. The following case fulfils these requirements.

Previous reports of this case have appeared, once in 1939 before the Philadelphia Dermatological Society<sup>2</sup> and prior to that by Herman and Lyon in 1921.<sup>3</sup> The present report summarizes the findings which appeared in these reports and the subsequent course.

### REPORT OF A CASE

J R, a Spaniard residing in Cuba from 1889 to 1906, suffered a severe burn with boiling oil, from which he recovered promptly, and contracted malaria, which lasted for months because of inadequate treatment, during the Spanish American War. Before that, in 1893, it was noted that he had a high erythrocyte count. In 1897 he had what was thought to be an attack of appendicitis and in 1900 an attack of renal colic, which was relieved when he passed several calculi. Another attack of renal colic in 1914 led to the discovery of a renal calculus. He refused operation until a third attack, in 1919, when his right kidney was removed at the Methodist Episcopal Hospital. At that time he was found to have an erythrocyte count of 11,400,000 per cubic millimeter, a leukocyte count of 11,600 per cubic millimeter and a hemoglobin content of 115 to 120 per cent (method not stated). No cyanosis, splenomegaly or other signs of polycythemia vera could be detected. After operation, his erythrocyte count dropped to 5,500,000 per

\* From the Ayer Clinical Laboratory of the Pennsylvania Hospital

1 Winer, L H. Local Amyloidosis of the Skin, Arch Dermat & Syph **23** 866 (May) 1931

2 Greenbaum, S S. Lichen Amyloidosis and Prurigo Associated at One Time with Pseudopolycythemia and Visceral Suppuration, Arch Dermat & Syph **39** 380 (Feb) 1939

3 Herman, L, and Lyon, B B V. Pseudopolycythemia. Extraordinary Blood Changes in a Patient with Renal Calculus, Ann Surg **73** 223 (Feb) 1921

cubic millimeter and his hemoglobin content to 108 per cent. Thirteen days after operation his leukocyte count rose to 260,000 per cubic millimeter for some unexplained reason. The differential count was as follows: polymorphonuclear neutrophils, 74 per cent, lymphocytes and monocytes, 17 per cent, and the remainder, basophils and eosinophils. His leukocyte count gradually fell to normal, and the erythrocyte count remained normal. At no time were any abnormalities noted in the shape and size of the erythrocytes. Pathologic examination of the right kidney indicated renal calculus with pyelonephritis and perinephritis.

In 1928, he was seen by one of us (S S G) because of an extensive, extremely pruritic papular eruption distributed over the lower extremities, which he stated had been present since 1918. A provisional diagnosis of lichen planus obtusus was made. Roentgenologic irradiation had no influence on the eruption. He was observed during 1929 and then not again by one of us (S S G) until 1938.

In the meantime (1934) he was admitted to the Pennsylvania Hospital because of partial urinary obstruction produced by an enlarged prostate with a large median lobe associated with prominent trabeculations and several small sacculations of the bladder. His urine was normal except for a few pus cells. The Wassermann reaction was negative. He stated that he had been well except for an attack of severe precordial pain and syncope which kept him in bed for a week about a decade before. A transurethral resection of 3 Gm of tissue from the neck of the bladder, consisting of hypertrophied nonmalignant fibromuscular tissue, relieved his urinary obstruction.

When seen in 1938 by one of us (S S G), he had pruritic, acutely developed strophulus-like lesions of the trunk. On the legs, particularly the outer surfaces, were many lesions similar to those seen in 1928. They were hard, discrete, pink, elevated papules from the size of a pinpoint to that of a pinhead after the scales covering them were removed to expose their smooth surfaces. Itching occurred when the parts were touched. Cutaneous scratch tests indicated faint susceptibility to flounder, herring, salmon, shad, lamb, liver, goat's milk, olives, oranges, peas, peaches, pecans and red and green peppers. A positive reaction was elicited to a local Congo red test. Histologic examination of one of the cutaneous lesions revealed amyloid infiltration of the papillary layer and hyperkeratosis. His blood cell count was normal. His urine contained a distinct trace of albumin and many leukocytes of unknown source.

On his final admission to the Pennsylvania Hospital, Oct 14, 1941, at the age of 72 years, he gave a history of intermittent claudication, dyspnea, edema of the ankles and oliguria of a year's duration. Administration of digitalis gave temporary relief. On physical examination, his temperature was normal, pulse rate 80 to 100 per minute, respiratory rate 20 per minute and blood pressure 210 systolic and 120 diastolic. He was well developed and well nourished, showing some respiratory distress. His heart was enlarged. A systolic murmur was heard at the base of the heart. Occasional extrasystoles were present. Rales were noted at the bases of the lungs. Edema of the legs extended to the thighs. Extensive cutaneous lichenoid eruptions associated with decided hyperpigmentation, especially at the sites of pressure, were noted. Electrocardiographic evidence of severe myocardial damage due to hypertension and coronary disease was obtained. He now had a slight anemia (4,200,000 erythrocytes per cubic millimeter and a hemoglobin content of 84 per cent). His urine contained a few hyaline casts, a trace of albumin and from 12 to 15 leukocytes per low power field. About ten days before death, a tender fusiform mass was felt in the epigastrium. He died instantly while straining at stool on Nov 17, 1941.

*Abstract of Necropsy* (performed by Dr Victor Karsis three hours after death)  
 —Externally a small, soft, pedunculated nodule, 8 mm in diameter, covered by smooth pink skin lay over the sternal region. The skin over the elbows and the knees was covered by several dry, elevated, fine, scaly plaques. Microscopically the growth over the sternum consisted of an encapsulated fibromatous nodule with fibers arranged in whorls. Sections of the skin from the legs exhibited discrete, homogeneous, pale eosinophilic, almost acellular, areas which occurred in the corium just beneath the epidermis. With Mayer's stain, these areas took the reddish violet hue characteristic of amyloid.

An extensive degree of arteriosclerosis involved the aorta and the coronary, splenic and iliac arteries. In the aorta, the intimal covering of many of the yellow atheromatous plaques was replaced by ulcers, on which were attached soft, friable, red-brown masses. The right renal artery was obliterated by a firm fibrous mass (the right kidney having been removed surgically years before). In the abdominal aorta just below it and in the orifice of the left renal artery was a fusiform aneurysm about 11 by 6 cm, which presented several ulcerations of the intima that had dissected the layers along the outer circumference of the aorta as far as the bifurcation and partly down the right iliac artery. The lumen of the right iliac artery was almost completely obliterated by a thrombus, and the lumen of the left iliac artery, greatly narrowed, appeared to communicate with the false lumen of the aorta. Saccular dilatations were present in the left iliac artery. There was no evidence grossly or microscopically that these changes were syphilitic in origin. The arteriosclerotic changes in the coronary vessels associated with calcification had produced sufficient narrowing of the lumens to lead to myocardial scars. The heart was enlarged, indicating some previous existence of hypertension since there were no valvular lesions other than mild sclerosis of age. The pulmonary conus was a trifle prominent. The lungs were emphysematous. The pulmonary vessels were unobstructed.

The spleen and liver were atrophied. The left adrenal was normal and the right partially atrophied. The left kidney, although showing evidence of previous compensatory hypertrophy, was nevertheless scarred by vascular changes. Punctate hemorrhages were scattered along the pelvis and ureter, which ran unobstructed to the bladder. The bladder was small and thick walled, with conspicuous trabeculations. Some ridges and scars lay in the region of the trigone and prostatic part of the urethra. The testes, epididymes, pancreas, thyroid, remnants of thymus, accessible lymph nodes, gastrointestinal tract and thoracic duct were not altered. The bone marrow from the lumbar vertebra was red and soft.

Microscopic studies of all the major organs failed to reveal any deposits of amyloid except in the skin. The lumbar bone marrow contained a few islands of erythropoietic and myeloid cells scattered throughout an abundance of fat.

The chief pathologic findings were extensive arteriosclerosis of the aorta, with a dissecting abdominal aortic aneurysm, arteriosclerosis of the left iliac artery, with small saccular dilatation, arteriosclerosis of the coronary arteries, with myocardial infarction of the posterior part of the right and left ventricular walls, arteriosclerosis generally, thrombosis of the right iliac artery and obliteration of the right renal artery, operative absence of the right kidney, absence of portions of the lateral lobes and the median bar of the prostate (transurethral resection), trabeculation of the bladder, pulmonary emphysema, arteriosclerotic scars of the left kidney, pedunculated fibroma of the skin over the sternum and primary amyloidosis cutis.

## COMMENT

Systemic amyloidosis secondary to chronic suppurative infections such as tuberculosis is common. Primary systemic amyloidosis, a form not associated with infections, multiple myeloma or tumors are distinctly uncommon. In 1939, Koletsky and Stecher<sup>4</sup> reviewed the findings in 24 cases and called attention to the occurrence of localized and systemic forms. In the localized variety, the amyloid was limited to one or possibly two organs or there was extensive involvement of one with slight and relatively insignificant deposits in other organs. Although they reported the occurrence of amyloidosis of the skin in 8 of the 24 cases, in none was this the only or the chief site of deposition. Recently Lindsay and Knorp<sup>5</sup> brought the study of primary systemic amyloidosis up to date by compiling the reports since Koletsky and Stecher's review. There are now 39 recorded cases of primary systemic amyloidosis, and in none was the disease confined to the skin.

The formation and deposition of that peculiar substance called amyloid because of its behavior with iodine and sulfuric acid and other stains is unexplained both in the secondary and in the primary form. It is apparent, however, from differences in staining qualities alone that amyloid is not a single substance but a complex variable substance or substances consisting of protein and polysaccharide fractions (Hass and Schulz,<sup>6</sup> Hass,<sup>7</sup> and Hass, Huntington and Krumdieck.<sup>8</sup> The pathogenesis of amyloidosis is still unknown, although it has been speculated that antigen-antibody reactions are incurred in its production. Such might conceivably be the case in chronic suppurative infections but would not be directly operative in the primary forms. In our patient, infection of long standing did not exist. The colon bacillus infection of the urinary tract disappeared when the right kidney was removed in 1919. Although it is possible that this infection may have existed for several years prior, it could not have been severe. Whether it had any relation to the papular eruption which was first noticed by the patient about the time of operation is doubtful. Moreover, there is no evidence that

4 Koletsky, S, and Stecher, R M. Primary Systemic Amyloidosis. Involvement of Cardiac Valves, Joints and Bones, with Pathologic Fracture of the Femur, *Arch Path* **27** 267 (Feb) 1939.

5 Lindsay, S, and Knorp, W F. Primary Systemic Amyloidosis, *Arch Path* **39** 315 (May) 1945.

6 Hass, G, and Schulz, R Z. Amyloid. I. Methods of Isolating Amyloid from Other Tissue Elements, *Arch Path* **30** 240 (July) 1940.

7 Hass, G. Studies of Amyloid. II. The Isolation of a Polysaccharide from Amyloid-Bearing Tissues, *Arch Path* **34** 92 (July) 1942.

8 Hass, G M, Huntington, R, and Krumdieck, N. Amyloid. III. The Properties of Amyloid Deposits Occurring in Several Species Under Diverse Conditions, *Arch Path* **35** 226 (Feb) 1943.

amyloid developed in the skin at this time, its presence having been recognized for the first time in 1939, long enough for the cutaneous disease itself to have been responsible for its formation. Since the history and necropsy findings gave no evidence of active chronic infection, one must conclude that the amyloidosis was not secondary to infection. Neither could it have been secondary to a neoplasm, for none was recognized at autopsy.

Amyloidosis secondary to multiple myeloma likewise could be dismissed on the basis of findings in the bone marrow at necropsy.

A further problem which remained unexplained was the polycythemia which existed prior to nephrectomy and then disappeared. No evidence of this disease existed during his several admissions to the Pennsylvania Hospital, and the lumbar bone marrow, normally rather active, was decidedly hypoplastic. It is questionable, too, whether this episode contributed to the formation of amyloid.

In primary systemic amyloidosis, a minimal deposit of amyloid in the liver, spleen, kidneys and adrenals occurs with a maximal deposit in the heart, lungs, skin and mucous membrane.<sup>5</sup> With the routine stains (hematoxylin and eosin) there were no changes in any of these organs to indicate special staining for amyloid. Hence, although it is possible that amyloid existed elsewhere in parts of the body that were not examined, such as the tongue, this seems improbable, because of the lack of symptoms referring to these parts, for example, macroglossia, nasal obstructions and sinusitis. We feel justified, therefore, in considering this a case of primary localized amyloidosis of the skin, cause unknown.

#### SUMMARY

A case of primary lichen amyloidosis with no evidence of amyloidosis elsewhere on postmortem examination is reported. A discussion of factors associated with primary systemic amyloidosis leaves the pathogenesis of this condition unexplained.

# Clinical Notes

## HYPERKERATOSIS OF THE PALMS AND SOLES DUE TO THE INGESTION OF QUINACRINE HYDROCHLORIDE

LESLIE PAXTON BARKER, M.D., NEW YORK

Recently there have been various types of cutaneous eruptions attributed to the ingestion of quinacrine hydrochloride (atabrine). Many of these eruptions have occurred in members of the armed forces serving in the Pacific, particularly in the New Guinea area. Cases of exfoliated dermatitis, giant urticaria, toxic erythema and certain kinds of lichen-planus-like eruptions have been reported. I believe that this is the first report of a case of hyperkeratosis limited to the palms and soles produced by quinacrine hydrochloride.

### REPORT OF A CASE

*History*—Major W. K., a 33 year old white man, first came to me for treatment of hyperkeratosis of the palms and soles on Dec 10, 1945. He had been in the Burma-India Theater of Operations from September 1944 until his return to the United States on Nov 1, 1945. He stated that he began taking quinacrine hydrochloride in September 1944, 1 tablet a day for the first seven days, 2 tablets a day for the next seven days and 1 tablet a day for the remainder of his stay abroad (fourteen months in all). About three months after use of quinacrine hydrochloride was started his skin became yellow, and in another three months thickened calluses began to develop on the palms. These calluses increased, eventually involving in a patchy fashion most of the palms. Two or three months later (eight or nine months after use of quinacrine hydrochloride was started) a similar hyperkeratosis appeared on both soles. This condition was symmetric and had at times developed fissures.

When the patient consulted me in December 1945, well defined patches of the hyperkeratosis were symmetrically distributed on the palms and soles. No horny plugs were present. The pressure areas were most severely affected, and the central part of the palms and insteps showed some involvement. The skin over the entire body was deep yellow but revealed no change in texture. There was no history of any ingestion of arsenic.

*Laboratory Findings*—Repeated scrapings from the hyperkeratotic areas of palms and soles revealed no fungi, and cultures for fungi showed no growth.

*Treatment*—Six per cent salicylic acid ointment was prescribed, to be applied night and morning to the hyperkeratotic areas. In addition, five weekly roentgen ray treatments (each 100 r) were given.

*Comment*—The aforementioned treatment apparently had no effect on the course of the disease, because it soon became evident that the hyperkeratosis lessened as the yellowish discoloration of the skin subsided. Now that the patient has not taken quinacrine hydrochloride for the past six months, only a slight discoloration and little hyperkeratosis remain.

### SUMMARY

The fact that this cutaneous eruption appeared and developed after a long period of intake of quinacrine hydrochloride (atabrine) and improved only as

the effects of quinacrine hydrochloride on other parts of the cutaneous surface lessened would indicate that the ingestion of quinacrine hydrochloride was the cause of the hyperkeratosis of the palms and soles

120 East Seventy-Fifth Street

## PSEUDOMONAS AERUGINOSA INFECTION OF THE EAR TREATED WITH STREPTOMYCIN

J LAMAR CALLAWAY, M D, DURHAM, N C

Infectious eczematoid dermatitis of the external ear often presents a difficult problem in therapy. The patient in the following case had a *Pseudomonas aeruginosa* infection of the external ear which was extremely resistant to treatment until streptomycin was used.

### REPORT OF A CASE

O K L, a 51 year old professor, was first seen on Aug 30, 1945 with an acute eczematoid dermatitis of the canal and pinna of the left ear. Culture revealed a pure growth of *Ps aeruginosa*. He was given the usual instructions for care of the ear, was told to avoid soap and water and was given 3 per cent salicylic acid in 70 per cent alcohol to apply locally twice daily, with application of a 3 per cent ammoniated mercury ointment at night. In addition he was given 50 r of superficial roentgen ray therapy. Because he did not improve under this therapy, he was admitted to Duke Hospital on September 9, where he remained for thirteen days. During that time a greenish yellow pus continued to exude from the ear. The severe eczematoid dermatitis of the canal and pinna responded poorly to all local therapy, including compresses, tincture of zephiran chloride locally, 1 per cent aqueous solution of gentian violet medicinal, Castellani's paint and penicillin ointment. In addition he received 1,000,000 units of aqueous solution of sodium penicillin intramuscularly. Throughout his entire stay in the hospital he was under the careful observation of an otolaryngologist. He improved somewhat and was discharged with directions to use 0.5 per cent and later 1 per cent weak solution of acetic acid as an irrigation and as instillation, but this was of little benefit.

Penicillin ointment and penicillin in aluminum hydroxide gel in a strength of 500 units per gram were used, without benefit. An autogenous vaccine, to which he gave a positive reaction after an intradermal test, was administered, without improvement, over a period of several weeks.

On April 19, 1946, eight months after onset, a culture of material from the ear again revealed a pure growth of *Ps aeruginosa*, and the ear remained eczematoid and exudative. An aqueous solution of streptomycin, containing 2,500 units per cubic centimeter, was prepared for instillation and as a sponging agent. Within forty-eight hours the oozing and erythema had subsided. The green purulent discharge stopped in two days, and cultures of material taken on May 1 and May 8, were completely negative for *Ps aeruginosa*. The ear was again examined by the otolaryngologist and found to be entirely normal.

This experience is reported with the hope that others may find this form of therapy helpful.

From the Division of Dermatology and Syphilology, of the Department of Medicine, Duke University School of Medicine

**DERMATITIS FROM GLASS FABRICS****LOUIS SCHWARTZ, M D, BETHESDA, MD**

Some months ago an outbreak of dermatitis was reported to the United States Public Health Service as occurring from women's suits and children's coats. Samples of the woolen material and the lining used in the women's suits accompanied the information. Examination of the materials showed that the wool was innocuous but that the lining was made of Fiberglass, which mechanically irritated the skin.<sup>1</sup>

Investigations in New York, where the suits were made, disclosed the fact that also among girls working on the lining dermatitis had developed, and the manufacturer was unaware of the fact that the lining was Fiberglass. The lining was thought to be rayon, which it closely resembled.

It was also learned that another manufacturer using this material as lining for babies' coats had been advised that outbreaks of dermatitis were occurring among babies who wore the coats.

The number of cases of dermatitis reported was so great that both the women's suit manufacturer and the babies' coat manufacturer were compelled to recall all the suits and coats, remove the lining and replace it with other fabric. The manufacturers stated that recalling and relining the garments cost around \$30,000. There still remain settlements to be made for damages to the sufferers.

Further investigation revealed that the fabrics had been purchased as surplus property from the government and that the purchaser knew that it was Fiberglass, but the manufacturers of the garments stated that they were not informed of this when they bought the material for linings.

The trade journals and the manufacturers of the Fiberglass fabric were notified of this outbreak of dermatitis, and a warning was given against use of Fiberglass for clothing. It was thought that this would end the matter.

Recently, however, reports have been received of dermatitis occurring from glass fabric being used for binding seams in women's dresses.

This report is made so that physicians will be on the lookout for and maybe able to make the diagnosis in other cases of dermatitis which may occur from irritation caused by Fiberglass in wearing apparel.

From the Office of Dermatology, Industrial Hygiene Division, Bureau of State Services, United States Public Health Service.

1 Schwartz, L, and Botvinick, I. Skin Hazards in the Manufacture of Glass Wool and Thread, *Indust Med* 12 142-144 (March) 1943.

**TINEA CAPITIS IN SOUTHEASTERN TENNESSEE****CLARENCE SHAW, M D, CHATTANOOGA, TENN**

From time to time various authors have reported the incidence of the types of organisms causing tinea capitis in different parts of the world. So far as can be determined there have been no published reports of this nature from this section of the United States. In the face of widespread epidemics of tinea capitis currently noted in other parts of the country it is thought worth while to record the character of the disease in this area.

Between July 1942 and February 1946, 22 consecutive patients with ringworm of the scalp have been seen from whom cultures of infected hairs were made. Three were Negroes and the remaining 19 were white. Their ages ranged from 2 to 9 years, 15 were boys and 7 were girls. The infections were from one week to twelve weeks in duration when first seen.

In 21 cases *Microsporum lanosum* was cultured, while in 1 *Trichophyton crateriforme* was isolated. Not a single example of *Microsporum audouinii* was encountered. The vast majority of patients cleared up within a few weeks with local applications of 5 per cent ammoniated mercury ointment. In most instances it was learned that the child had played with a kitten or a puppy shortly before the onset of the scalp lesions. Clinically, many of the affected areas closely resembled the classical picture of infection with *M. audouinii*. Had the appearance of the lesion been the sole criterion for the type of treatment to be used, several would have been needlessly epilated with roentgen rays.

#### SUMMARY

Twenty-one out of 22 patients with ringworm of the scalp were infected with *M. lanosum*, the culture for 1 patient showed *T. crateriforme*. No examples of infection with *M. audouinii* were found, which emphasizes the value of culture studies.

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#### CORRECTION

In the report of the March 21, 1945 meeting of the Chicago Dermatological Society (*ARCH DERMAT & SYPH* 54 744, 1946), the word "correct" in the ninth line from the bottom of page 746, in Dr. Zakon's discussion of the paper by Dr. Frederick R. Schmidt, "Chronic Discoid Lupus Erythematosus," should read "incorrect."

# Abstracts from Current Literature

EDITED BY DR HERBERT RATTNER

TROPICAL ANIDROTIC ASTHENIA (THERMOGENIC ANHIDROSIS) AND ITS RELATIONSHIP TO PRICKLY HEAT MARION B SULZBERGER, H M ZIMMERMAN and KENDALL EMERSON, JR, J Invest Dermat 7 153 (Aug) 1946

A typical case of tropical anhidrotic asthenia observed on Guam is reported. The clinical and histologic observations indicated that this disease and ordinary prickly heat are different manifestations of the same fundamental process.

The authors advanced the hypothesis that the sensory disturbances in prickly heat are due to the distention and changes of pressure produced by the secretions of sweat into the plugged ducts and that these symptoms vanish in tropical anhidrosis as the result of the rupture of these ducts allowing free drainage of sweat into the surrounding tissues. Biochemical studies led to observations indicating that the principal systemic manifestations present in this disease are due to hyperventilation as well as to defects in the cooling mechanism of the skin.

An attempt was made to remove the obstructions from the sweat ducts by peeling the skin with ultraviolet light. A return of normal sweating was observed in several portions of the desquamated areas. The patient made a complete recovery in about two months on his return to a temperate climate.

THE TREATMENT OF PYODERMAS WITH AN INTERFACE ACTIVE SOLUTION OF TYROTHRICIN GEORGE M MACKEE, MARION B SULZBERGER, FRANZ HERRMANN and FLORENTINE L KARP, J Invest Dermat 7 175 (Aug) 1946

The purpose of this investigation was to study the clinical response of a variety of pyodermic diseases to a stable 0.1 per cent solution of tyrothricin in a vehicle capable of penetration into the skin. The solution was applied byunction and in the form of wet compresses in full strength or in dilutions with one or two parts by volume of boiled tap water.

A favorable clinical response was noted in 232 patients with various cutaneous diseases caused or complicated by pyogenic infection. Included among patients giving favorable response were 112 patients with various types of acne vulgaris.

THE CYTOLOGY OF MOLLUSCUM CONTAGIOSUM WITH SPECIAL REGARD TO THE SIGNIFICANCE OF THE SO-CALLED "VACUOLES" E MEIROWSKI, S KEYS and G BEHR, J Invest Dermat 7 165 (Aug) 1946

The authors present their observations through a series of semischematic drawings to prove that the so-called vacuoles in molluscum contagiosum are not true vacuoles but spherical bodies resulting from the response of the epidermal cell to a virus stimulation.

These bodies appear first within the nucleus and are then extruded into the cytoplasm where they increase in size and number and coalesce to form a large single "H-P" body, containing numerous surface compartments.

SOME NEWER BASES FOR USE IN CUTANEOUS THERAPY J G HOPKINS, J Invest Dermat 7 171 (Aug) 1946

The author presents three types of bases which offer the advantages that the ingredients are all relatively inert and do not react with the constituents of tissue.

The first, an ointment base, consists of a series of polyethylene glycols. They are marketed under the trademark name "Carbowax Compound". By the mixture of Carbowax having molecular weights of 1,500 and 4,000 with propylene

glycol, ointments of any desired consistency can be prepared. This base is an excellent solvent not only for water-soluble substances but also for numerous organic compounds such as sulfonamide compounds, salicylic acid and penicillin. They are convenient for application to the scalp because of the ease with which they can be washed out.

The second base is a bentonite gel and is prepared by mixing 10 to 20 per cent of bentonite with water. The addition of talc facilitates the formation of a smooth gel and the addition of propylene glycol prevents the gel from drying out. Substances such as oils, fats, lecithin or petrolatum emulsify easily in this gel to produce an emulsion having excellent lubricating qualities. This base is suitable for water-soluble drugs such as sodium penicillin, sulfonamide compounds, fatty acids and salicylic acid, as well as the insoluble powders such as sulfur, ammoniated mercury and zinc oxide.

The third, carnauba wax, when mixed with cerasin and liquid petrolatum makes a base which adheres well to the skin, hardens its surface and repels water. Such cerates are useful as vehicles for active ingredients soluble in oil, such as salicylic acid, chlorophenols or chrysarobin.

IDENTIFICATION OF THE INHIBITORY FACTOR OF RETICULO-ENDOTHELIAL IMMUNE SERUM (REIS) IN A GLOBULIN FRACTION. EDWARD H. FRIEDEN, C. M. POMERAT and LUDWIK ANIGSTEIN, *Science* **102** 354 (Oct. 5) 1945

The authors have been able to isolate the albumin and the globulin fractions of reticuloendothelial immune serum by saturating the serum with ammonium sulfate and dialyzing against cold Tyrode's solution until the fluid is sulfate free.

Preliminary experiments demonstrated the following results:

"The albumin fraction obtained from homologous (anti-chick) REIS with a complement fixation titer of 1:1,200 showed no inhibition of outgrowth from fibroblasts or from splenic fragments.

"The globulin fraction, on the other hand, inhibited the outgrowth of fibroblasts and produced clumping of splenic cells to approximately the same degree as controls containing an equal dilution of corresponding REIS.

"Globulin fractions of heterologous (anti-rat) REIS with a complement fixation titer of 1:1,600 did not produce such inhibitory effects on chick tissues *in vitro*."

Attempts to develop a method of measuring the potency of globulin fractions of the reticuloendothelial immune serum as to both their inhibitory and their possible stimulating action and further fractionation of the globulins are under study.

PATHOLOGIC FINDINGS IN A CASE OF AINNUM. COMPARISON OF THE EPIDERMAL AND VASCULAR LESIONS WITH THE NORMAL TOE. VERNON E. MARTENS and ROBERT F. NORRIS, *U. S. Nav. M. Bull.* **45** 745 (Oct.) 1945

Ainnum occurring in a Negro veteran 50 years of age is described, in which the essential lesion appeared to be chronic osteomyelitis. The hyperkeratinization and the hypertrophy of the media of the small arteries previously reported as characteristic of this disease were present in sections taken from 4 grossly normal toes which had been removed from dead white servicemen. The authors suggest that the fibrous constriction of the little toe is not the cause of the destruction of bone but is the result of cicatrization of previously inflamed tissue.

The article includes a review of the literature and several photomicrographs of the pathologic and the normal sections of the toes.

SIMULATING SERUM-SICKNESS REACTION TO PENICILLIN. WILLIAM E. SULLENS, JR., *U. S. Nav. M. Bull.* **45** 752 (Oct.) 1945

The author reports that penicillin produced an allergic reaction which simulated serum sickness. The symptoms consisted of giant urticarial lesions on the abdomen, the back and the hips, arthralgia of the wrists and the ankles, moderate edema of the feet and the hands, a temperature of 99 F, headache and a moderate general lymphadenopathy occurring six days after a second course of penicillin treatment.

Intradermal tests with a 1:10 solution and a 1:100 solution of calcium penicillin in isotonic solution of sodium chloride produced no reactions at the sites of injection, however, multiple small areas of urticaria appeared above these areas five hours later. The author was unable to determine whether the reaction was due to penicillin or to an impurity of the product.

TOXIC EFFECTS OF ARSENICAL COMPOUNDS AS ADMINISTERED IN THE UNITED STATES NAVY IN 1944, WITH SPECIAL REFERENCE TO ARSENICAL DERMATITIS  
OTTO L. BURTON, GEORGE W. JUSTYN and LAURA T. ANDERSON, U. S. Nav M. Bull. 45:783 (Oct.) 1945

In 1944 medical officers of the Navy administered a total of 396,144 doses of arsenical compounds. A total of 381,475 injections of oxophenarsine hydrochloride were given, resulting in 67 reactions, of which 5 were fatal, giving a ratio of reactions to doses of 1 to 5,694 and a ratio of deaths to doses of 1 to 76,295. A total of 12,398 doses of neoarsphenamine were given, resulting in 13 reactions, of which 3 were fatal, giving a ratio of reactions to doses of 1 to 954 and a ratio of deaths to doses of 1 to 4,133.

Arsenical dermatitis constituted 32 per cent of the total reactions and was of the following types: exfoliative, macular, erythematous, urticarial, papular, maculopapular, morbilliform, pustular and vesicular. Premonitory signs were present in many cases, and this fact suggests the necessity of careful examination and questioning of each patient before an arsenical drug is administered.

ANAPHYLACTOID (SANARELLI-SHWARTZMAN) REACTION FOLLOWING THERAPEUTIC ANTITYPHOID INJECTIONS  
JULIAN LOVE and RICHARD H. DRISCOLL, U. S. Nav M. Bull. 45:1108 (Dec.) 1945

A fatal reaction occurred in a young white man following a second intravenous injection of antityphoid vaccine given within a twenty-four hour interval as non-specific therapy.

At autopsy the finding of petechiae throughout the parenchymal organs and brain and of massive necrosis of the liver and the kidneys indicated a general anaphylactoid reaction. The authors state their belief that the pathologic changes are similar to those obtained by Sanarelli and Schwartzman in experimental animals.

The reaction can be avoided by allowing an interval of at least forty-eight hours between injections.

CASE OF KERATODERMIA BLENNORRHAGICUM (GONORRHEAL DERMATITIS)  
JOHN R. GATELEY, U. S. Nav M. Bull. 45:1159 (Dec.) 1945

A case of keratosis blennorrhagica is reported, in which the patient was observed and treated aboard a carrier in the Pacific. This patient, a young white man, presented a classic clinical picture characterized by articular pains, headache, fever, slight urethral discharge and symmetric bilateral eruptions of the skin of the hands and the feet, the lesions developing into vesicles and pustules with incrustation and pseudokeratinization. A history of sexual intercourse, leukocytosis (10,500 cells), a temperature of 101° F and the recovery of gonococci from cutaneous lesions aided in establishing the diagnosis.

The disease was treated by internal administration of sulfathiazole and application of silver nitrate (10 per cent) to the local cutaneous lesions.

SKIN LESIONS OF RHEUMATIC FEVER  
ALEX. D. CAMPBELL, GEORGE C. GRIFFITH and WILLIAM H. LEAKE, U. S. Nav M. Bull. 46:360 (March) 1946

This discussion of the cutaneous manifestations of rheumatic fever is based on observations made by the Rheumatic Fever Unit stationed at the United States Naval Hospital, Corona, Calif.

Erythema annulare rheumaticum of the Lehnendorff and Leiner type was the most common lesion encountered. Certain other erythematous eruptions, subcutaneous

nodules and purpura were also found to be specific for rheumatic fever. Erythema nodosum and erythema multiforme were found to be nonspecific.

Erythema annulare rheumaticum was not invariably associated with valvular heart disease and did not have prognostic significance.

It was the authors' impression that more urticaria was present in their patients with rheumatic fever than ordinarily found in their other hospitalized groups.

RODIN, South Bend, Ind

HERPES ZOSTER AND CHICKEN-POX. JAMES TAYLOR, Brit M J 2:385 (Sept 22) 1945

Dr Taylor points out the fully established connection between herpes zoster and chickenpox. He contends that there is sufficient evidence to justify making herpes zoster a notifiable disease.

THE INITIAL TREATMENT OF TROPICAL ULCER. F. E. STOCK, Brit M J 2:388 (Sept 22) 1945

An effective treatment for tropical ulcer is described by Stock. On three successive days the ulcer is painted with a saturated solution of potassium permanganate, which is allowed to dry. Undermined skin at the edge of the ulcer is trimmed off with scissors and painted with the same solution. The whole surface is then dusted lightly with pure iodoform and covered with cotton. At the end of three days any of the familiar treatments with antiseptics, ointments, occlusive dressings or skin grafts can be employed.

HAEMOLYTIC DISEASE AND CONGENITAL SYPHILIS IN SIBLINGS. MARJORY N. McFARLANE, Brit M J 2:494 (Oct 13) 1945

The author reports on a family which provides information on the supposition that congenital syphilis may cause erythroblastosis. The blood of the mother, aged 34, was group A<sub>1</sub> and Rh negative (rr). Her husband was overseas. In 1935 the patient gave birth to a premature living baby girl whose blood was of group A<sub>1</sub> and Rh positive. In 1939 she was delivered of a full term baby boy who died of icterus gravis neonatorum (hemolytic disease, type II). In 1941 she had a miscarriage at six months. The fourth pregnancy resulted in a full term living baby girl whose blood was of group O and Rh negative.

In the second child erythroblastosis was present, but evidence of syphilis was lacking. The presence of powerful anti-Rh agglutinins may reasonably be supposed to have been responsible for the fetal hemolytic disease and possibly for the subsequent miscarriage. The outcome of the fourth pregnancy, however, indicates that evidence of syphilis may be present in the mother and infant without fetal erythroblastosis, even in a family in which hemolytic disease has previously appeared. Hemolytic disease did not develop in this child in spite of strong anti-Rh agglutinins in the mother's blood, owing to the lack of the Rh-positive antigen in the fetal cells.

There is at present no satisfactory evidence to show that congenital syphilis or other infection can bring about by itself the clinical and pathologic features of fetal erythroblastosis, and blood group incompatibility is the only proved cause of this neonatal disorder.

REHABILITATION OF PATIENTS SUFFERING FROM SKIN DISEASE. R. MASON BOLAM, Brit M J 2:539 (Oct 20) 1945

In 1943, seventy beds were allocated for the rehabilitation of patients in dermatologic cases among military personnel. During two years 800 men have been admitted, 584 of these have been returned to duty and 216 have been discharged from the service.

Patients with many types of cutaneous disease apart from those of a chronic, widespread, intractable nature will benefit from rehabilitation, and much can be

done by showing the patient how to live with his disease and how to apply his treatment correctly

The psychiatric aspects of these patients deserve detailed study since a considerable number are poorly adjusted, displaying anxiety to a varying degree, whereas others have a pronounced self-centered disposition. During the period of convalescence the utmost tact and sympathy are necessary in handling special cases in which it must be decided whether a man may resume his former occupation or should engage in work along new lines. Facilities provided include woodwork, leatherwork or needlework, entertainment, a library, educational courses, lectures and the opportunity to work on the grounds and the farms in the neighborhood.

Types of cutaneous diseases which benefit from rehabilitation of the patients are (1) dermatitis seborrheica, (2) eczema, (3) impetigo, (4) pyodermitis, (5) furunculosis, (6) dermatitis due to a sulfonamide compound and (7) lichen planus.

In treating dermatitis seborrheica of the trunk and the extremities, the authors have found the following prescription far superior to the more popular sulfur-salicylic acid ointment:

Solution of coal tar N F	} 1 drachm (3.88 Gm or Cc) of each
Prepared calamine N F	
Zinc oxide	
Peanut oil	
Petrolatum to make 1 ounce (30 cc)	

An interesting observation is the fact that men recovering from dermatitis due to a sulfonamide compound are unable to wear khaki clothing, necessitating testing of the skin with uniform material before they are returned to the service. The author recommends that rehabilitation of patients with cutaneous disease should be introduced for the civil population.

SHAW, Chattanooga, Tenn

#### PATHOGENESIS OF ENCEPHALITIS DUE TO SALVARSAN STEPHAN VON PASTINSZKY, *Dermatologica* 87 12 (Jan) 1943

Two young men, one with primary and secondary syphilis and the other with a syphilitic chancre, were treated with a bismuth compound and mild doses of neoarsphenamine (0.3 to 0.45 Gm every four days). After four intravenous injections in the one case and three in the other severe encephalitis developed, which in 1 instance was associated with dermatitis due to arsphenamine. The patients recovered. The serum of the 2 patients elicited positive Prausnitz-Küstner reactions in test persons and passive anaphylaxis against arsphenamine in rabbits. The results of the tests, the accompanying dermatitis and the onset after small doses are considered as evidence that the encephalitis is due to hypersensitivity to neoarsphenamine.

#### EXPERIMENTAL STUDIES ON THE QUESTION OF THE CAUSE OF PEMPHIGUS HULUSI BEHÇET, BERTA OTTENSTEIN, GUZIN TOKSOY and SATI ESER, *Dermatologica* 87 113 (March) 1943

The authors tried to duplicate Lindenberg's experiments on animals, which seemed to prove the viral nature of pemphigus. They inoculated 19 rabbits with blood serum, blister contents and brain emulsion from 4 patients with pemphigus and 1 with epidermolysis bullosa hereditaria. These test materials were introduced by intratesticular, epidermal, intracutaneous and subcutaneous routes. During an observation period of two months no animal showed any pemphigus-like lesions of the skin.

#### HISTOLOGIC FINDINGS AND HERZBERG'S STAIN FOR VIRUS IN PEMPHIGUS PERIHAN CAMEL, *Dermatologica* 87 127 (March) 1943

Three male patients who died of pemphigus showed at autopsy microscopic hemorrhages of the brain, increased pigmentation of ganglions, fatty degeneration

of the liver and lack of cells of the splenic pulp These signs are regarded as infectious-toxic, others—for instance, bronchopneumonia—are regarded as secondary complications Two patients showed fibrosis of the testes, 1 of whom had in addition chronic thyroiditis of the Riedel type Herzberg's stain did not reveal any virus

ERYTHROPLASIA OF THE GLANS PENIS (BOWEN'S DISEASE OF THE MUCOUS MEMBRANES) L M PAUTRIER, *Dermatologica* 87:169 (April-May) 1943

Pautrier has always maintained that erythroplasia of Queyrat and Bowen's disease of the mucous membranes are identical

He reports on a 57 year old man with oozing tender bright red lesions of the glans penis and some slightly infiltrated papillomatous lesions of the corona glandis In this case the erythroplasia started with lesions similar to those seen in balanitis circinata erosiva Two or three small lymph nodes were palpable in the inguinal area The histologic examination revealed changes characteristic of Bowen's disease

The author regards this condition and others of the same sort not as precancerous but as truly epitheliomatous, requiring surgical intervention

A NEW TYPE OF GRANULOMATOSIS WITH GENERALIZED TUMORS SIMULATING MYCOSIS FUNGOIDES WITH FATAL OUTCOME L M PAUTRIER, *Dermatologica* 87 190 (April-May) 1943

A 37 year old man had almost generalized soft, red-brown, partly ulcerating tumors which looked clinically like mycosis fungoides The histologic examination, however, revealed a different picture The tumors consisted of lymphocytes and cells which were hard to classify but which looked like young histiocytes The patient also had obstructing tumor masses inside the nose and an ulcer of the epiglottis He suffered from bilateral tuberculosis of the pulmonary apexes The blood picture ruled out leukemia Aleukemic leukemia did not seem probable

This, in the author's opinion, is another case of the group entitled "non-classifiable granulomatosis," a term which he introduced in 1937

A PECULIAR FORM OF SKIN ATROPHY W LUTZ and H PICARD, *Dermatologica* 88 79 (Aug) 1943

Since the autumn of 1941 a 17 year old girl has shown on her extremities livid noninfiltrated discolorations which are either circumscribed and of round or oval shape or confluent and forming a bizarre bandlike pattern She does not recall any exposure to intense cold The lesions feel doughy, the overlying skin gradually becomes as thin as cigaret paper Before the terminal stage of atrophy is reached, one finds edema and widening of the papillary layer of the corium, widening of the increased blood vessels and marked dilatation of the lymph spaces but no inflammatory infiltration The livedo-racemosa-like design speaks against primary macular atrophy and acrodermatitis atrophicans chronica, the distribution, however, suggests a functional disturbance of the blood vessels as the underlying etiologic factor

MELANOTIC NEVUS OF THE CHEEK, APPARENTLY UNDERGOING MALIGNANT DEGENERATION, DUE TO A LARGE UNDERLYING FOREIGN BODY GRANULOMA WHICH HAS DEVELOPED AROUND BONE FORMATION L M PAUTRIER, *Dermatologica* 88:110 (Aug) 1943

A 44 year old woman had had since infancy three pigmented nevi of the right cheek During eight weeks the largest of the lesions became tender, elevated and infiltrated A diagnosis of nevus-epithelioma was made All nevi were removed with the electric cutting current The changes observed histologically were those of a nevus, without signs of malignant changes, and of an enormous foreign body granuloma which had developed in the deep part of the corium and subcutis around

some osseous formation A rudimentary sebaceous cyst might have caused the metatypic bony growth The author feels that the constant irritation underneath the nevus would sooner or later have caused malignant degeneration of the nevus

**LEUKODERMA ACQUISITUM CENTRIFUGUM (SUTTON) AND THE REPRODUCTION OF THE PRESENTATION OF SIMILAR CUTANEOUS CHANGES ON A PANEL OF THE ALTAR OF ISENHEIM** H KUSKE, *Dermatologica* 88 282 (Nov-Dec) 1943

The author reports 4 new cases of leukoderma acquisitum centrifugum In the course of his studies of this disease he observed on a panel of the altar of Isenheim, which depicts the temptation of St Anthony, a demon showing cutaneous changes characteristic of leukoderma acquisitum centrifugum (This is not the man covered with tumors, which are manifestations either of leprosy or of syphilis) It is, of course, doubtful whether Grunewald had ever seen a human model exhibiting numerous pigmented spots surrounded by depigmented areas

**ATYPICAL CHONDRODYSTROPHIA OF THE TYPE MORGUINO ASSOCIATED WITH FOLLICULAR ATROPHODERMA** G MIESCHER, *Dermatologica* 89 38 (Jan-Feb) 1944

A 6 year old girl showed at birth beginning kyphoscoliosis and other signs of chondrodystrophia fetalis calcaria This disturbance is accompanied with a tendency of the skin toward follicular atrophy There are many areas of pseudopelade on the scalp Changes of the skin of the trunk and the extremities resemble atrophoderma vermiculatum of the face In this case, however, the face is not involved

**EXTENSIVE PAGET'S DISEASE WITHOUT FORMATION OF CANCER DURING CONSTANT OBSERVATION FOR FOURTEEN YEARS** G MIESCHER, *Dermatologica* 89 45 (Jan-Feb) 1944

The cutaneous disease of a 42 year old woman started with a pinhead-sized red fissure of the right nipple fourteen years previously, after the birth of a child Two years later, on histologic examination the diagnosis was Paget's disease of the epidermis and the milk ducts At the time of the author's last observation the whole right breast and the adjacent parts of the trunk were covered with oozing, eroded and crusted confluent lesions A movable soft small gland could be felt in the right axilla A second histologic examination, in 1943, showed the same classic polymorphous Paget's cells as did the first biopsy The disease at the time of the author's last observation involved also the orifices of the sebaceous glands Fractional doses of roentgen rays and subsequently grenz rays for recurrences at the periphery brought about complete epithelization of the eroded area

**BOWEN'S DISEASE (WITH RARE LOCALIZATION BETWEEN THE SECOND AND THE THIRD LEFT TOE)** P ROBERT, *Dermatologica* 89 55 (Jan-Feb) 1944

For three years a 47 year old man noticed in the second interdigital space of his left foot itching rhagades, which were unsuccessfully treated as intertriginous and mycotic eczema The verrucous, thickened, sharply circumscribed lesion showed histologically the typical epidermal changes of Bowen's disease

**URTICARIA PIGMENTOSA OF PECULIAR, LIVEDO-RACEMOSA-LIKE DESIGN** W STALDER, *Dermatologica* 89 72 (Jan-Feb) 1944

Two years ago a 19 year old woman noticed on the inner surface of the thighs reticular confluent hyperemic and edematous streaks, which later flattened They assumed a brownish-blackish color Exposure to cold and rubbing caused edematous swelling Needle pricks were followed by local highly red urticarial elevations which spread to neighboring streaks Areas farther away also became elevated The histologic examination showed numerous chromatophores and small perivascular infiltrations of lymphocytes and scanty mast cells in the papillary

layer In the corium there also were occasionally some perivascular mast cells A diagnosis of cutis marmorata pigmentosa was ruled out The scant presence of mast cells, even their absence, does not speak against urticaria pigmentosa in the opinion of the author and other dermatologists whom he mentions

A CASE OF TRICHOFOLLICULOMA G MIESCHER, *Dermatologica* 89 193 (April-May) 1944

For a year a 46 year old woman with a few pigmented nevi and small angiomas on her face had noticed on her right cheek a small nodular elevation, from the center of which a tuft of hair emerged Whenever she pulled out some hairs, some serum exuded from the same opening After extirpation of the tumor the histologic examination revealed an enormous follicular orifice with about eighty lanugo hairs There were many secondary follicular pockets present, all hairs, though, left the skin through the same orifice Sweat glands and signs of inflammation were missing

A NEW TYPE OF FAMILIAL AND HEREDITARY AGENESIS AND DYSTROPHY OF THE HAIR ALICE ULLMO, *Dermatologica* 90 75 (Aug-Sept) 1944

The father and the grandfather of a boy and his sister, described in detail, seemed to have shown identical malformations Eyebrows, eyelashes and axillary and pubic hair were missing The son had no beard The scalp showed tonsure-like alopecia of the central parts, while the rest of the hair of the scalp was black and thick There were small keratotic follicular plugs disseminated over the entire body The teeth and the nails, however, were not deformed The girl suffered from psychosis, and the boy was mentally retarded

CONFLUENT ERUPTION OF VERRUCAE PLANAE OF THE HANDS, THE FOREARMS AND THE NECK, SIMULATING EPIDERMODYSPLASIA VERRUCIFORMIS, ASSOCIATED, HOWEVER, WITH VERRUCAE VULGARES L M PAUTRIER, *Dermatologica* 90 86 (Aug-Sept) 1944

For five or six years a 33 year old man has suffered from verrucae planae spreading over the dorsal surfaces of his hands, his forearms, his face and his neck There are large verrucae vulgares on the dorsa of the fingers and over the metacarpophalangeal joints

The abundance of the small lesions which, by the way, surpass the size of ordinary verrucae planae suggests epidermodysplasia verruciformis, the coexistence of vulgar warts and the histologic structure of the smaller lesions, however, only permit a diagnosis of verrucae planae Only few cells show vacuolation of malpighian cells The author raises the question whether there are perhaps not fundamental but quantitative differences between epidermodysplasia verruciformis and verrucae planae

CAUSE OF PHAGEDENIC SOFT CHANCRE. N MELCZER, *Dermatologica* 90 157 (Oct) 1944

In order to solve the question why a soft chancre occasionally becomes phagedenic, pus from a phagedenic chancroid was inoculated into the skin of the same patient or into that of healthy persons Invariably, phagedenic ulcerations were produced In smears of pus or scrapings from phagedenic chancroids, streptobacilli, other bacteria and the elementary bodies of a filtrable virus were seen If filtrates containing the pure virus alone or pus alone were inoculated into animals, negative results were obtained Filtrates containing the virus were rubbed into scarified skin of healthy persons or intracutaneously injected No ulcers resulted If, however, mixtures of the filtrate with various strains of bacteria were inoculated, or if the filtrate was implanted in pyodermic lesions, phagedenic ulcerating lesions developed These phagedenic pyodermic lesions could be transmitted to other test persons

HELEN O CURTH, New York

# Society Transactions

## NEW YORK DERMATOLOGICAL SOCIETY

Hans J Schwartz, M D, *President*

George C Andrews, M D, *Secretary*

May 22, 1945

### A Case for Diagnosis (Ichthyosis Hystrix? Psoriasis?) Presented by DR A BENSON CANNON

R O, a 9 month old white Italian boy, was born at full term with normal delivery and was apparently healthy except for an eruption which occupied the same sites and distribution as at present. The lesions have become more scaly and of a darker red color. The diet has consisted of evaporated and goat's milk reenforced with vitamin D, without any apparent change in the disease. The mother thinks that orange juice aggravates the eruption. There are no subjective symptoms.

Examination shows a healthy-looking, well developed child with numerous red, linear, macular lesions in wavelike formation, covered with gray scales in layers. The eruption is most pronounced on the sides of the body, the back and the sides of the face. Long, wide bands, 6 to 8 inches (15 to 20 cm) in length by several inches in diameter, are noticeable along the lines of the ribs. Numerous red, scaly plaques resembling psoriasis are noticed in the scalp, with apparently normal skin between the plaques. There were no changes in the nails.

Scrapings from the lesions were negative for fungus.

#### DISCUSSION

DR JOHN C GRAHAM The linear character of the lesions plus the fact that they have been present since birth would, in my opinion, make ichthyosis hystrix the diagnosis of choice.

DR EUGENE F TRAUB The distribution on the trunk, where whirls can be seen, is certainly a congenital anomaly, but the eruption is not sufficiently cleancut for ichthyosis hystrix, and in a patient of this age one has to wait until further development before coming to a final conclusion.

DR MAURICE J COSTELLO I think that the eruption is nevroid in character. I saw a case similar to this, in which the eruption was much more extensive, consisting of streaks of telangiectasis.

DR FRED WISE I have the impression that the lesion is a nevus.

DR HOWARD FOX There is no doubt about this being a generalized, linear nevus. The question of psoriasis being present since birth is unusual. I have never heard of a case like that.

### A Case for Diagnosis (Linear Nevus? Lichen Planus Atrophicus?) Presented by DR MAURICE J COSTELLO

L D, a 6 year old girl, was first seen by me on May 3, 1945, when she showed a generalized scratched, papular, urticarial eruption. Examination at that time showed another eruption, entirely different in type, involving the left lower extremity, which her mother stated had been present about three years and was zosteriform in distribution, extending from the mid thigh to the calf, and more prominent on the lateral aspect. The individual lesions varied from the size of a matchhead to that of a half dime and were sharply margined. Some of the lesions

were red and others hyperpigmented, with depressed centers Examination with a magnifying glass showed the center of the lesions to be atrophic and studded with tiny follicular plugs Many of the lesions were discrete, but some were coalesced to form bizarre patterns

## DISCUSSION

DR. FRED WISE The lesion appears to me to be a linear nevus Histologic changes often simulate the appearance of chronic lichen planus in eruptions of this character, and the scarring is produced by involution of the lesion

DR A BENSON CANNON I favor the diagnosis of lichen planus She has lichenoid, shiny papules on the margin of the involved areas which look strikingly like lichen planus

DR LESLIE M SMITH (by invitation) I rather think that it is atrophic lichen planus

**Nevus Pigmentosus** Presented by DR PAUL E BECHET.

J O, a woman aged 47, stated that she had a single papillomatous pigmented nevus between two toes of her left foot, which had been present since birth There has been a rapid increase in size in the past five years She was sure that it had doubled in size There were no subjective symptoms

The lesion has a mulberry-like appearance with considerable pigmentation It is somewhat pedunculated and measures approximately 15 mm in length by 9 mm in width The patient is presented for discussion as to whether the lesion should be removed or left in situ

The patient also has an ordinary contact dermatitis on her face and neck, which is irrelevant to the presentation

## DISCUSSION

DR MAURICE J COSTELLO I think that this is a simple pigmented nevus and can easily be removed without risk to the patient

DR. LESLIE M SMITH (by invitation) I should destroy the lesion by electro-coagulation

DR JOHN C GRAHAM I agree that it is benign and perfectly safe to remove.

DR HOWARD FOX This is a soft pigmented nevus, with a pedicle showing its benign nature It could be removed even without anesthesia, following which the base could be thoroughly cauterized

DR FRANK C COMBES I wonder what the pigment is

DR PAUL E BECHET I am deeply grateful for the discussion and shall remove the lesion My reason for the presentation was to ascertain the opinion of the society as to the advisability of intervention Many years ago, a patient with a lesion in the same location was presented before the Manhattan Dermatologic Society by the late Dr Oulmann The majority of dermatologists present at the meeting advised against its removal Some years later Dr Oulmann reported to the society that the patient had had the lesion excised by some one else and had died within the year from multiple metastases The relation of this tragic occurrence impressed me with the necessity of extreme caution in deciding whether or not to remove the type of growth presented by the patient under discussion

**Generalized, Progressive Scleroderma Associated with Changes in the Lungs, the Larynx and the Esophagus** Presented by DR HOWARD FOX

M G, aged 47, a salesman, was first seen by me on July 9, 1937 Six months previously, following an attack of influenza, he began to have general malaise and first noticed changes in the skin These changes were limited to the hands and the upper part of the chest and clavicular region The hands and fingers were swollen and the overlying skin moderately hidebound There was no tapering of the fingers and no history or signs of Raynaud's disease The fingers had a peculiar yellowish

color The upper part of the chest and clavicular region were somewhat shiny and striated, the upper portion presenting short, parallel, white ridges, varying from  $\frac{1}{8}$  to 1 inch (0.3 to 2.5 cm) in length The lower part of the area showed patchy pigmentation and some depigmentation The skin in these areas was definitely ludebound The finger nails showed longitudinal ridges and furrows and a tendency to be convex anteroposteriorly as well as laterally

A general physical examination, made just previously at the Mount Sinai Hospital (Consultation Service), showed no abnormalities except scleroderma and some unidentified roentgenologic changes in the lungs

The patient's chief complaints were a dry, hacking cough and dyspnea on exertion He was advised to do no work and to live in a warm climate For the past eight years he has spent much of his time in Florida or southern California His cutaneous lesions do not bother him and have not increased in extent or severity in the past eight years The hoarseness of voice, dry cough and dyspnea on exertion have gradually become worse

For the past few years he has been under the care of Dr James Alexander Miller, who wrote in December 1941 "I have about finished my study of Mr M G Investigation of his respiratory function was made at the Presbyterian Hospital by Dr Richards He reported the unusual finding that with perfectly adequate ventilation the patient showed striking oxygen deficiency on moderate exercise and also was unable to absorb inhaled oxygen to relieve such deficiency Dr Richards says that this would be perfectly consistent with the diagnosis of pulmonary fibrosis involving the alveoli rather than the peribronchial tissue, and that is just what I think this man has" In a recent letter (May 17, 1945) Dr Miller added that "in addition to a bilateral pulmonary fibrosis, he also has a dilated esophagus and a certain amount of cardiospasm A bronchoscopic examination shows a thickening of the mucous membrane of the larynx and trachea, characteristic of scleroderma" Also, Dr A Wilbur Duryee took an electrocardiogram and encephalogram in May 1943, which "showed a disturbance of the cortex such as is found in 80 per cent of the cases of scleroderma"

#### DISCUSSION

DR FRED WISE The coincidence of pulmonary fibrosis in association with progressive scleroderma has been emphasized in several recent publications

DR MAURICE J COSTELLO I saw this man some years ago, when I was associated with Dr Howard Fox, and at this time, in addition to beginning difficulty in breathing, he also had difficulty in swallowing, which he now claims has cleared up I think that his dyspnea is due to true pulmonary fibrosis in addition to restriction of respiratory movement caused by infiltration of the muscles of the skin

DR GEORGE M LEWIS A patient recently studied at the New York Hospital showed the site of the sclerosing process to be in muscles predominantly rather than in the skin

DR HOWARD FOX The involvement of the respiratory tract is extremely unusual I have seen many cases of progressive scleroderma, and I have never seen a case like this and do not know whether such has ever been presented before the society This man has pulmonary as well as laryngeal and esophageal involvement There was no cancer, as one physician at the Misericordia Hospital thought He has been treated with an enormous amount of vitamins of all kinds, and lately he has been taking oxygen, which seems to help him That is the only treatment he is receiving

#### A Case for Diagnosis (Lupus Erythematosus? Pemphigus?) Presented by DR FRANK C COMBES

M G, a man aged 60, was referred to me with the diagnosis of pemphigus, it impressed me rather as being lupus erythematosus, with lesions of the lips and oral mucosa predominating The patient's health has always been good except that diabetes was discovered four months ago, his fasting blood sugar content being

230 mg per hundred cubic centimeters at that time. In July 1944 he noticed a bluish white line on his lower lip. Some time later scaly patches developed on his forehead. Two months later an erosion appeared on the left side of his lower lip, which responded to treatment with radium. Two similar lesions were destroyed by electrodesiccation.

At present there are three nummular, erythematous patches on his forehead, partially covered with a dry, adherent scale. In some areas the surface is glazed and atrophic, the scale tending to be attached at the borders. On the buccal mucous membrane on the right side is an erythematous patch. On the lips are several crusted erosions. The vermilion borders of the lips are poorly defined, and in some places there are bluish white areas of hyperkeratosis and hemorrhagic crusts.

#### DISCUSSION

DR MAURICE J COSTELLO: If I had one diagnosis to make I should say lichen planus. The lesions on the buccal mucosal membrane and border of the lip suggest this disease.

DR A BENSON CANNON: I think that it is a most unusual case and that the diagnosis would rest between lupus erythematosus and lichen planus. I feel much as Dr Costello does, that if I had to choose between the two I should probably choose the latter. The patient has an extensive involvement of the mucous membranes, the vermilion border of the lips and the lower part of the entire mucous membranes of both cheeks, more especially the right, he has linear and circinate white lesions that look much as though he had them painted with silver nitrate, and he even has lesions of the hard palate. The red area on the right side of the forehead could well be lichen planus. I think that the final diagnosis rests on histologic study, one section from the forehead and one from the mucous membranes of the mouth.

DR HOWARD FOX: Often when a diagnosis seems to lie between lupus erythematosus and lichen planus, after the case has been sufficiently studied, it is apt to be proved to be lupus erythematosus. Between these two I should favor lupus erythematosus.

DR FRED WISE: I strongly favor the diagnosis of pemphigus, which at present appears to be in a mild form but may at any time flare up into severe pemphigus vulgaris, with fatal results. A fair proportion of the Senear-Usher eruptions terminate in pemphigus vulgaris, ending in death.

DR ANTHONY C CIPOLLARO: This is a confusing clinical picture, and I doubt that one biopsy specimen will tell the story. I think that the patient should be thoroughly studied, and several biopsy specimens from various areas will be required before a diagnosis can be made.

DR FRANK C COMBES: I saw this patient this morning for the first time. He was sent in with a probable diagnosis of pemphigus, and naturally my efforts were all toward disproving that diagnosis. The symptoms seem to me to point to lupus erythematosus. I cannot see lichen planus as the diagnosis, but if I had to choose between lichen planus and pemphigus I should choose the former.

#### Mycosis Fungoides Presented by DR FRANK C COMBES

In H. W., a man aged 61, there have for the past six years developed irregularly shaped, bizarre, erythematous patches on various parts of his body, which have remained more or less fixed and have been accompanied with no subjective symptoms other than occasional, inconsequential pruritus. On the right elbow are cicatrices designating the site of two bean-sized nodules removed for histologic examination. One nodule on the right wrist was irradiated. All erythematous patches have faded somewhat after irradiation therapy. At present the lesions are situated on his arms, thighs and buttocks and average 15 cm in diameter. They are flat, the borders are festooned, the erythema is of varying intensity, in places

they are telangiectatic and they do not disappear entirely on pressure. In some sites there are areas of skin of normal color, roughly eiremate, varying in size up to 2 cm. In a few areas there is a suggestion of deep nodule formation and scaling. The eruption is roughly symmetric.

Examinations of the blood have given constantly normal results. Histologic examination of the nodules and erythematous patches have suggested nothing but a benign granuloma and chronic inflammatory tissue respectively, although clinically it had been my impression that mycosis fungoides was the correct diagnosis. One of the nodules recently removed from his elbow showed the typical polymorphic infiltration characteristic of this dermatosis. The Wassermann reaction of the blood was negative.

#### DISCUSSION

DR MAURICE J. COSTELLO: I think that this patient has mycosis fungoides.

DR ANTHONY C. CIPOLLARO: I agree with the diagnosis.

DR HOWARD FOX: I agree with the diagnosis.

DR FRED WISE: On clinical grounds, I favor the diagnosis of mycosis fungoides.

DR LESLIE M. SMITH (by invitation): I believe that this is mycosis fungoides or some other member of the lymphoblastoma group.

DR FRANK C. COMBES: I am glad that the majority of opinion is in favor of mycosis fungoides. This man's condition has grown progressively worse, although individual lesions have responded temporarily. I hesitated to make a definite diagnosis because the changes were so uniform and the cellular infiltration so uniform, both suggesting a condition much more benign in nature than mycosis fungoides. However, as time goes on, I believe that there will be changes typical of this disease. The erythematous lesions show some slight improvement, the lesion on his wrist, which was a nodule about 2 cm. in diameter, received 150 r and resolved in two weeks.

#### Postarsphenamine Vitiligo Presented by DR A. BENSON CANNON

H. O., a white housewife aged 47 years, was admitted to Vanderbilt Clinic on Dec. 27, 1943, suffering with generalized postarsphenamine dermatitis of three weeks' duration. She married at the age of 21, lived with her husband three months and had one miscarriage. The husband was found to be syphilitic. The patient had no treatment until seven months ago, since which time she has had two injections of neoarsphenamine and one injection of a bismuth preparation each week until the outbreak of the present eruption. Her skin has been red and crusted, oozing, burning and itching, accompanied with much swelling of the face and lower extremities. She has felt extremely weak and has had nausea.

General examination showed a well developed and nourished woman in considerable distress. The skin was universally red, scaling and crusted. The feet, legs and areas around the orbits were considerably swollen.

Laboratory tests showed a high blood arsenic content, of 0.15 mg. per hundred grams of dry specimen. Several subsequent tests were also high for arsenic. The urine was essentially normal, as was the blood cell count, except for a slight leukocytosis. The Wassermann and Kline reactions of the blood were negative, and the spinal fluid was normal. The complete chemistry of the blood was essentially normal.

Treatment consisted of daily injections of sodium thiosulfate and later of calcium thiosulfate, 250 mg. of vitamin C was given daily, and 4 cc. of crude liver was given intramuscularly twice a week for about three months. The patient gradually improved, both in physical well-being and in the appearance of the skin. Eventually the skin was entirely free from dermatitis. As the eruption cleared, white spots were noted all over the body and extremities, with an apparent increase of pigment surrounding the white areas. The patient's skin is dotted all over with pea-sized to silver dollar-sized white macular spots.

## DISCUSSION

There was no discussion of this case All agreed with the diagnosis

### Exudative Discoid and Lichenoid Chronic Dermatitis Presented by DR FRED WISE

J W, a boy aged 15, was seen at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on July 6, 1944, presenting lesions of nine months' duration The father is Jewish and the mother Gentile There is no allergic history in the family or in the patient He had the first attack two weeks after moving into a new apartment Intradermal tests of all the common allergens were said to give negative results He complains of severe itching Because of this and the disfigurement caused by the appearance of the lesions, mental symptoms developed and he threatened to commit suicide

He was hospitalized at the Kings County Hospital, where he received eight injections of typhoid vaccine He improved while there but had a relapse soon after his discharge from the hospital He was also treated with nine injections of Hapamine (a chemical combination of histamine and despeciated horse serum globulin), without benefit

The patient presents a generalized, dusky, erythematous, oozing, eczematized eruption on the trunk and extremities The lesions are elevated and consist of matchhead-sized to split pea-sized macules, discrete and coalesced, forming ill defined circular and oval plaques and bizarre-shaped patches Many of the lesions are excoriated and covered with crusting and scaling They are more pronounced on the cubital and popliteal areas, where they are arranged in a circular fashion As in all eruptions of this kind, the skin of the penis is involved

The patient was ordered to receive the following treatments baths in a solution of potassium permanganate, phenobarbital, 25 mg, and thiamine hydrochloride, 5 mg, each three times a day, and testosterone propionate, 25 mg, by intramuscular injection three times weekly

## DISCUSSION

DR HOWARD FOX Some call this disease discoid eczema I think that this case falls into the class that Rosen first described and later was studied by Sulzberger and Garbe

DR A BENSON CANNON I agree with Dr Fox and the presenter that this is a classic example This is the youngest patient I have ever seen, and I have been observing such cases since 1916 I think that this is a contact dermatitis and that he can get absolute cure by a change of environment

DR LESLIE M SMITH (by invitation) Most of you are probably familiar with the fact that about a year ago the El Paso Chamber of Commerce mailed to a good many of the dermatologists in the East copies of their weekly bulletin, advising that patients with disseminated neurodermatitis be sent to the Southwest to be treated by sunshine We of the El Paso medical profession do not approve of this type of publicity and do not feel that our climate is the answer to the problem of neurodermatitis, and we have requested that the Chamber of Commerce discontinue this publicity I have seen the majority of the cases of neurodermatitis and chronic discoid lichenoid dermatosis which the publicity man had in mind Many of the patients have improved, some after a few weeks, but more of them after a prolonged rest, while some have received no benefit or have gotten worse I feel sure that the change of environment and the rest from nervous strain at home have more to do with the benefit than the dry air and sun I believe, however, that, particularly in the cases of exudative conditions, there is a benefit from the dry air and cautious sun bathing in some of the cases

DR MAURICE J COSTELLO I agree with the diagnosis

DR FRANK C COMBES I agree with the diagnosis The problem in these cases is the origin of the lymphadenopathy This patient also has enlargement of all his superficial lymph nodes This adenitis in many cases is a simple irritative

phenomenon I have followed several patients and found the histologic picture to change to giant follicular lymphadenopathy and later polymorphous cell sarcoma, with a fatal outcome. Favorable response of the dermatosis to treatment will check this metamorphosis. Best results have followed a change of environment. Other medical therapy has given unsuccessful results, except temporary improvement following radiotherapy to the nodes.

DR FRED WISE This is the youngest patient afflicted with this dermatosis that I have encountered. The eruption appears to occur almost exclusively in male Jewish patients.

#### Lupoid Sycosis Presented by DR FRED WISE

G F, a man aged 24, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on May 22, 1945, presenting lesions of one year's duration. He gives no history of previous disorders of the skin.

A small pustule first appeared on the right cheek. A month later many more pustules developed in the same area in a circular manner. The rest of the bearded region then became affected. He was treated in the Army with penicillin salve and with injections of penicillin every three hours continuously for fifteen days, for a total of one hundred and twenty injections, without any apparent improvement. A silver dollar-sized area on the right cheek was then exposed to roentgen rays for "ten minutes," the rest of the face being shielded with lead. This was not followed by any inflammatory reaction. Most of the hair in the irradiated area has not regrown since. He was then sent to Walter Reed Hospital, where he was treated with ammoniated mercury salve, alcohol and boric acid soaks and with other salves, without result. The patient stated that the bald spot on the right side of the cheek has the same appearance as before the roentgen ray exposure except for the lack of growth of hair.

On the right cheek, along the mandible and extending below to the neck is a fairly well defined patch, 7 by 4 cm in diameter, which is erythematous, almost entirely denuded of hair growth, atrophic and revealing fine folds. The entire bearded region, including the front and sides of the neck and the upper lips, is also affected with numerous follicular pustules pierced by hairs and covered with crusting and scaling.

The routine laboratory tests gave normal results.

#### DISCUSSION

DR HOWARD FOX I am surprised that penicillin has not done him any good. I have seen a number of articles that speak highly of the use of penicillin in sycosis.

DR EUGENE F. TRAUB Before the diagnosis of lupoid sycosis is finally accepted, the question of the single ten minute dose of radiation has to be considered, because this may possibly be a case of loss of hair follicles. In regard to penicillin therapy, I had an experience with a case of sycosis recently, of eleven years' standing, in addition to folliculitis, involving the hair of the forearms of five years' duration. This patient was given penicillin locally. He seemed to be much irritated after this particular variety of penicillin was applied, and I thought that he was possibly sensitive to the vehicle, so I incorporated the next batch in Aquaphor. He kept getting progressively worse during the period in which penicillin was applied to the skin. He was then treated by injection in the usual manner, and after the first one or two injections he swelled up to twice his size and became so violently ill that treatment had to be discontinued. In this case of sycosis vulgaris the penicillin seemed to be actually an irritant.

DR JOHN C. GRAHAM I have had the same experience as Dr. Traub with penicillin in sycosis. I have a patient who was irritated by penicillin ointment. However, he is now using tyrothricin in liquid form and is tolerating it well.

DR A. BENSON CANNON I hope to show 2 patients in parallel cases of general sycosis, 1 treated with sulfathiazole locally and the other with penicillin injection,

and both patients were cured. One is going about now without a lesion. This is the most beautiful cure I have ever seen from use of two different drugs, and I could not tell the difference in the beneficial effect between the two.

DR GEORGE M LEWIS I have recently seen two eczematous reactions to the local application of penicillin.

DR MAURICE J COSTELLO In my experience the local application of penicillin has been gratifying. It would be most unusual if there were not some people who were not sensitive to a new medicament. A specialist in pulmonary disease told me that in patients given insufflations of penicillin and oxygen there occasionally developed dermatitis venenata of the perioral regions and generalized urticaria and angioneurotic edema later. In the patients found to be sensitive to penicillin, I should like to suggest the application of Quinolor Compound Ointment (10 per cent benzoyl peroxide and 0.5 per cent Quinolor [a mixture of 3 chlorine derivatives of 8-hydroxyquinoline] in a base of equal parts of petrolatum and wool fat).

DR PAUL E BECHET The condition struck me as an ordinary sycosis and the atrophy and superficial scarring on both cheeks a possible radiodermatitis. If I understand the history correctly, the patient told Dr Wise that he had received a ten minute exposure to roentgen rays. I should like to testify that I have also had excellent results with Quinolor, but I have also seen it fail in a few cases. On the whole, however, it has, in my experience, proved of great value in the treatment of this obstinate dermatosis.

DR FRANK C COMBES I do not think that we should talk so glibly of the effect of penicillin locally in pustular dermatoses. In sycosis vulgaris there are many factors which must be considered, including the type of organism, the susceptibility of the person, his type of skin and associated disease. The question also arises, why has this patient lupoid sycosis rather than sycosis vulgaris? Is it a peculiarity of the infectious agent or the person? Probably the former is *Staphylococcus albus*. It has been my practice when giving penicillin to follow it either with penicillin by mouth or with toxoid injections. In spite of this, relapses are common in sycosis.

DR FRED WISE The patient never suffered from a reaction produced by the topical use of penicillin. There is no evidence of alopecia or dermatitis caused by roentgen ray treatment. The atrophic area and alopecia are manifestations of lupoid sycosis.

#### A Case for Diagnosis (Mycosis Fungoides? Arsenical Dermatitis?) Presented by DR GERALD MACHACEK

S M, a Negro woman aged 35, shows an eruption of four years' duration, which began on the sides of the trunk as pigmented spots that did not itch. At that time she was taking Ex-lax and Feen-a-mint. She received some intravenous injections from a local physician, following which she began to itch all over. So far as she knows, the Wassermann reaction of the blood was negative before these injections were started and has always been negative.

On entering Vanderbilt Clinic on Jan 6, 1944, she showed a symmetric generalized eruption involving the trunk and extremities but not the hands, feet, face or scalp. The lesions are deeply pigmented, elevated patches, palm sized and smaller. Some are gyrate or configurate in shape. Many plaques are infiltrated, and some are scaly. A biopsy specimen showed psoriasiform dermatitis with a possibility of premycotic mycosis fungoides. Dried blood showed 0.22 mg of arsenic per hundred grams. The Wassermann and Kline reactions of the blood were negative. Examination of the blood showed a hemoglobin content of 11.9 Gm (82 per cent), 4,350,000 red blood cells, 5,300 white blood cells, polymorphonuclear leukocytes 68 per cent, leukocytes 29 per cent, and eosinophils 3 per cent. The serum cholesterol level was 174 mg per hundred cubic centimeters. Cephalin flocculation was normal.

The patient was treated with injections of calcium and sodium thiosulfate without any beneficial effects. Fractional doses of roentgen rays were slightly beneficial. Dental roentgenograms and examination showed nothing abnormal.

Laboratory examination gave these results: plasma vitamin C, 13 mg per hundred cubic centimeters; serum phosphatase level, 22 mg; inorganic phosphatase level, 34 mg; and urea nitrogen content, 12 mg; there was a faint trace of bilirubin. The serum protein content was 61 mg; albumin content 42 mg; globulin level 19 mg; and urea nitrogen content 7 mg per hundred cubic centimeters. The erythrocyte sedimentation rate was 35 mm in one hour. A roentgenogram of the chest was normal. The patient received intravenous injections of typhoid vaccine, with no appreciable change in condition. While in the hospital she had an attack of blepharoconjunctivitis, with fever, and perirectal abscess.

A second biopsy, done on Aug 29, 1944, showed lymphoblastoma (mycosis fungoides). A third biopsy specimen of the papular lesions on the chin showed "tuberculosis cutis."

NOTE—This case was previously presented at the New York Academy of Medicine, Section of Dermatology and Syphilis, in February 1945, by Dr Gerald Machacek.

#### DISCUSSION

DR MAURICE J COSTELLO: I agree with the diagnosis.

DR PAUL E BECHET: On the back, in the scapular areas, the lesions are circinate.

DR ANTHONY C CIPOLLARO: I cannot offer any diagnosis, but I certainly do not think that this is a clearcut case of either mycosis fungoides or arsenical dermatitis. The diagnosis depends on the histologic changes. Further studies and observation will no doubt reveal the true nature of this disease.

DR HOWARD FOX: I agree that the condition in this case is a difficult one to diagnose, but I am surprised that no one has made the attempt to find fungus microscopically or by culture. I suggest that such examinations be made.

#### Contact Dermatitis of the Hands Presented by DR FRANK C COMBES

S S, a dentist aged 51, has had a dermatitis of both hands for over two years. It has varied in severity, at times involving only a few areas on the backs of his fingers. For four months following its inception it was confined to the second finger on the right hand. At the present time it involves all the fingers, and there is some scaling of the palms. Scrapings have been persistently negative for fungi. There is no evidence of a fungous infection or of any focal bacterial infection in his teeth, tonsils or sinuses. He has a reaction (2 plus) to a trichophytin test but gives a history of tinea capitis at the age of 8. Patch tests with 2 per cent procaine hydrochloride on two occasions have elicited negative reactions.

#### DISCUSSION

DR ANTHONY C CIPOLLARO: I do not believe that this is contact dermatitis. I think that this man has an eczematous eruption belonging to the group of localized, atopic dermatitis or nummular eczema. I have had similar cases, and all efforts to ascertain the cause have been fruitless. It is significant that this patient has lesions even when away from his work, a fact which favors the diagnosis of localized atopic dermatitis.

DR A BENSON CANNON: I agree with the presenter that this is contact dermatitis, probably occupational, and the solution of the problem depends on the detective work with sensitization tests of the skin.

DR EUGENE F TRAUB: More consideration should be given to the question of fungous infection as a factor in this case. He might have nail involvement, he has a positive trichophytin reaction, which is a point in favor of fungous infection. He has lesions of a vesicular character, which are not common except in rare cases.

of atopic eczema or dermatitis of the hands. This may explain why the eruption does not entirely disappear when he is on a vacation. There is no doubt that he has a dermatitis superimposed on this, and my feeling is that most dentists are difficult to treat and keep on one form of treatment consistently. I believe that they will try to use various medicaments, and this, too, may be a factor in the chronicity of this case.

DR GEORGE M LEWIS. I believe that there is probably a contact causation in this case. I agree with Dr Traub that it is extremely difficult to keep dentists on a strict regimen as regards exclusion of possible sensitizers.

DR MAURICE J COSTELLO. If this patient were not a dentist, I wonder whether the question of contact dermatitis would come up at all. I agree with Dr Cipollaro.

DR FRANK C COMBES. I agree that persons do not just contract contact dermatitis. It depends on three factors, namely, cellular susceptibility and exogenous and endogenous factors. Undoubtedly in this instance, some constitutional factor is present. It may be a good idea to have him see an allergist. There is no doubt that he is suffering from a neurosis, and I agree with Dr Lewis and Dr Traub that he has just enough knowledge of medicine to make him meddle with himself. Even tonight he stated that when he covers his lesions with collodion he feels better, also when he puts them into extremely hot water it relieves the itching.

#### CLEVELAND DERMATOLOGICAL SOCIETY

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May 24, 1945

**Erythema Chronicum Migrans** Presented by DR H N COLE and DR J R DRIVER

W S, a white woman aged 56, was born in the United States. Three years ago a red ring developed on the anterior surface of the neck. Later two similar lesions appeared. All three have gradually enlarged and become confluent. She has used iodine locally. Recently a new lesion has appeared just below the confluent lesions.

On the front of the neck is a thin, raised, firm, red, serpiginous lesion in a roughly circular outline, representing the coalition of several lesions. The lesion is slightly indurated and slightly raised above the surface. Below it there is a nickel-sized annular area, flat in the center. There is no scaling and no vesicle formation. The hemogram and urinalysis gave normal results. A roentgenogram of the chest showed calcified foci. The maxillary sinuses showed thickening of the mucous membranes. There was arthritis in the sacroiliac joints and of the spine.

The biopsy specimen was unsatisfactory. At one end was epidermis of five to eight cell thickness with a slight cellular infiltrate around the vessels in the corium. The endothelial cell lining of the vessels was swollen. The other portion of the section showed the epidermis to be much lower, and the underlying tissue shows swollen, collagenous fibers. There was no evidence of giant cell formation. Collagen tissue was not fragmented.

#### DISCUSSION

DR H N COLE. There seems to be a slight amount of atrophy in the center of the area, and I am sorry that we did not take a specimen from it also for examination, to see what it would show. I think that one would have to consider the possibility of sarcoidosis, though I never have seen a sarcoid with such a fine line as this patient shows. Usually, when there is an annular type of sarcoid,

there is more atrophy than we find in this patient. As far as she knew, she had never been bitten by a tick.

The patient did have tuberculosis, which apparently is healed.

One would consider granuloma annulare and a gyrate type of chronic erythema, but the line is too fine for the latter.

In 1909 Afzelius reported a case similar to this before the Stockholm Dermatological Society, and in 1911 Balban (Balban, W. *Arch f Dermat u Syph* 105:423-430, 1911) reported before the Vienna Dermatological Society an erythema annulare, with epithelial cell, typical of what is found in this case. All Balban's 3 patients had been bitten by wood ticks. That was also true of the patient in Afzelius' case (Afzelius, A. *Acta dermat-venereol* 2:120-125, 1921).

Lipschutz in 1913 reported cases (Lipschutz, B. *Arch f Dermat u Syph* 118:349-356, 1913), the disease is usually spoken of after him, "erythema migrans of Lipschutz." However, it was not reported originally by him. Lipschutz considered that this is a rare disease, and it is in this country, though apparently in Sweden there are cases occasionally. It is, of course, a well forested country. Perhaps that has something to do with it, as Afzelius pointed out. The narrow line that is found is fine, slightly raised and of a pinkish color. There is a little evidence of atrophy in the center. It usually starts with a single spot and then spreads. This peripheral type of spread in the case Lipschutz reported reached a diameter of 50 cm, an extensive process on one thigh, so they do get to be of large size and they may last for several years. In 1 patient of Balban's, it lasted for a year.

It is difficult to conceive how this process could follow the bite of a wood tick. It has been compared, also, with swine erysipelas, but in that disease there is not the picture seen here. Moreover, there are chronic manifestations which these patients never have.

**Parapsoriasis.** Presented by DR. H. N. COLE, DR. J. R. DRIVER and (by invitation) DR. A. R. MINADEO.

F. W., a white girl aged 18, is employed as a photographer. There is no history of any similar disease in the family. The patient stated that she perspires little except on the face, even in hot weather. She has always been well. She has been troubled since she was 4 years old, and perhaps earlier, with an eruption, which is persistent but worse in the summertime. There is no pruritus in connection with it.

There is a generalized eruption made up of plaques that are not particularly well defined, covered with red, silvery scales. In some places, scaling is more prominent than in others, e. g., over the thighs the scaling is much more extensive and almost confluent. The face is exempt. On some areas there is no scaling, but there is a retiform type of brownish pigmentation with a certain amount of atrophy. This is particularly noticeable in the inner aspect of the upper part of the arms and the inner aspect of the thighs. The hair, lips, teeth and nails seem to be normal. There is no evidence of involvement of the mucous membranes.

A histologic report of skin from the back by F. D. Weidman, University of Pennsylvania, is as follows:

In specimen A the stratum corneum was not clearly defined as such, because its cells merged insensibly with those below. For the most part, they were barely recognizable. The granular layer was not thick. The epidermis, as a whole, was moderately thickened. The interpapillary pegs extended to uniform depths, and, although they merged from place to place and broadened, they still maintained a regularity of character. The prickle cells were of young type, as indicated by their richly chromatinized nuclei. Basal cells were active and frequently underwent metaplasia into prickle forms. Some of the prickle cells toward the surface showed intracellular edema, and the same was true along the basement membrane.

In the corium there were no pronounced pathologic changes, excepting in the center of the lesion. A narrow zone of inflammatory change could be traced

immediately below the epidermis throughout the entire section. It consisted of hyperplastic capillaries and lymphocytes, with a few polymorphonuclear leukocytes. The nuclei of the few fibroblasts present were pyknotic. Sweat glands were not exhibited, and elastic tissue was absent except for a few delicate strands under the epidermis.

Specimen B was from the medial surface of the arm. The picture in this specimen was entirely different from that in the preceding specimen. The epidermis was atrophic and did not exhibit tendencies to parakeratosis. Immediately below the epidermis appeared a fairly broad zone of loosely fibrillar tissue containing numerous small capillaries, a few chromatophores and scattered fibroblasts and lymphocytes. The picture was that of young scar formation or residual fibrosis.

The eruption has been resistant to external treatment, including much superficial roentgen irradiation.

**Parapsoriasis en Plaque** Presented by DR H N COLE, DR J R DRIVER, and (by invitation) DR A R MINADEO

R S, a white woman aged 21, is an office worker. She has not had any previous cutaneous disease, and there was no history of a similar disease in the family. In the winter of 1943 an eruption developed on the arms, and this later spread to the legs and trunk. There is little pruritus with it. The patient has always had much dandruff. She occasionally takes Ex-lax. She is a well developed and nourished person.

There was extensive pityriasis of the scalp at the time of examination on Dec 29, 1944. There is an eruption that is made up of lesions that are sharply defined and have a tendency in places to assume an arciform shape. They are superficial and present on the arms, trunk, thighs and neck. In some places they are confluent. If anything, the lesions are more extensive on the extensor surface than on the flexor surface. There is some enlargement of the lymph nodes. A salicylic acid lotion was prescribed for the scalp and a tar and ammoniated mercury ointment for the skin.

#### DISCUSSION OF THE TWO PRECEDING CASES

DR E W NETHERTON. In the case F W, I thought that some of the lesions on the arms were suggestive of parapsoriasis. However, the other lesions were more inflammatory than is usual in the plaque type of parapsoriasis. The scaling of the lesions on the arms and the legs was superficial and, in many respects, was similar to that of parapsoriasis.

In case R S, I thought of a fixed drug eruption. Some of the lesions had a variation in color. The lesions in the groin were almost purple, and the lesions on the lateral trunk were oval and had a play of color from a deep violet at the periphery. There was pigmentation on the back that looked like that of a fixed drug eruption.

DR H HECHT. In regard to R S, I think that it is a drug eruption due to phenolphthalein.

In case F W, if the parapsoriasis started at the age of 4, it would be rare. Although I suppose that it is possible, I do not think that it is parapsoriasis. If one had examined this patient without knowing the history, one would say it is an allergic eruption. The patient stated that she had many dermal diagnostic tests without results. I still think that it must be an allergic eruption that started at the age of 4.

DR H N COLE. I believe that these patients have been receiving ultraviolet irradiation over a period. This has changed the appearance since December 1944. In both those cases, I believe that chronic resistant macular and maculopapular scaly erythroderma would have to be ruled out. Certainly, the girl who has had the eruption since she was 4 years old has not been taking phenolphthalein all those years. I do not know any other entity which would fit in so well here as parapsoriasis.

R S has some itching now, but it has been present only since she has been getting irradiation with the quartz lamp

DR A R MINADEO (by invitation) Dr Cole misunderstood me in regard to the ultraviolet irradiation R S has had about ten treatments with an Alpine lamp, with some improvement F W had no treatment, with the exception of rose water ointment U S P

DR BENJAMINE KLINE Do you regard the condition in R S as parapsoriasis as well as that in F W?

DR H N COLE I do

**Urticaria Pigmentosa (Nodular Type)** Presented by DR H N COLE, DR J R DRIVER and (by invitation) DR A R MINADEO

K B is a white girl aged 9 months The parents are living and well Nobody else in the family has had a similar disease When the patient was 6 months old, the mother noted a spot on the side of the baby New lesions have continued to develop, and all have persisted The baby does not seem to be scratching She eats a large amount of carrots

Scattered over the neck, trunk and shoulders are ovoid, raised, nodular, yellowish brown lesions Many of them are smooth, others have an irregular surface The palms have a yellowish brown color, and the cheeks have a slight yellowish tinge

The histologic section showed a low epidermis Changes of pathologic character were limited to the upper dermis The lower dermis was normal There was a diffuse stroma in which there were many cells with a deeply staining nucleus and a large light pink surrounding cytoplasm There was no evidence of inflammatory reaction With polychrome methylene blue stain, typical mast cells were seen There were many open spaces between the cells There was no giant cell formation Fat stains were negative for xanthoma cells

#### DISCUSSION

DR A R MINADEO (by invitation) I saw this girl about three weeks ago for the first time There was fine vesiculation on a few of these nodules The mother stated that this had occurred on previous occasions

DR D R PRINTZ I read the articles by Graham Little (*Brit J Dermat* 17 355, 1905, 20 232, 1908) and also the American literature on this subject Dr Little described a nodular type of urticaria pigmentosa This case duplicates his entirely After the lesions are stroked, a fine erythema appears, especially at the base

At one time it was thought that the pigment in urticaria pigmentosa was due to the mast cells In this case, although the cells were high up in the dermis, there was even more infiltration around hair follicles and the sweat glands, which is characteristic of urticaria pigmentosa

DR J E RAUSCHKOLB I was struck with the color of the baby, which probably modified the lesions of urticaria pigmentosa somewhat The baby has been ingesting large amounts of carrots and her skin has a Chinese yellow color Many of the nodular lesions are yellow, and I think that the disorder is carotenosis of the skin

**A Case for Diagnosis (Epidermodysplasia Verruciformis?) Chronic Myeloid Leukemia** Presented by DR G W BINKLEY

D M H, a white woman aged 44, consulted me in May 1940 for an eruption on the hands, which had appeared two years earlier There were no antecedents who had this condition

The primary lesion is a small, flat, angular, red-brown papule There are many of these on the dorsa of the wrists and fingers and the extensors of the forearms The papules may be single but usually are found in small groups In these groups

there is a tendency to confluence There are a few ring forms and parts of rings  
A chronic myeloid leukemia was discovered three years ago

The urinalysis showed normal findings A Kline exclusion test of the serum gave a negative reaction Many hemograms were made

### Results of Hemograms

	Erythro cytes	Hemo globin, Gm	Leuko cytes	Neutro phils, %	Eosino phils, %
11/13/42	4,220,000	11	47,000	65	4
3/22/45		12.5	12,200	61	5
	Baso phils, %	Lympho cytes	Mono cytes	Myelo cytes	Myelo blasts
11/13/42	7	8	2	13	1
3/22/45	4	23	7	0	0

A histologic examination of a typical papule showed a thick layer of loosely attached hyperkeratosis A papule was made up of a well defined area of acanthosis and an infiltrate in the underlying corium In the involved area the stratum granulosum was thicker than normal The cells of the upper rete showed liquefaction of the cytoplasm The nuclei of these cells were larger than normal Such changes were severe near the stratum granulosum and less severe in the middle portion of the rete However, there was some spongiosis of the basal cell layer Blood vessels in the corium were dilated and surrounded by a cuff of lymphocytes

Use of yellow mercurous iodide, 0.01 Gm three times daily for twenty days, was the first treatment In June 1940 cautery removal of all visible lesions was performed, with prompt recurrence In 1942, six or seven fractional doses of superficial roentgen irradiation were administered to the upper extremities at the Cleveland Clinic There was no change Finally all lesions were refrigerated with liquid nitrogen The eruption has slowly progressed

Deep roentgen irradiation was given to the front and back of the chest and abdomen for leukemia

### DISCUSSION

DR H J PARKHURST I could not differentiate the individual lesions clinically from juvenile flat wart, as their mold and order of appearance were similar, and I will have to be persuaded that was not what they were

DR H N COLE The fact that the lesions were present only on one hand to any extent would be more in favor of flat warts

DR H G MISKJIAN I had the same impression, and I was taking the presenter's diagnosis lightly However, after seeing the histologic picture and finding it was so characteristic, I now think that it is epidermodysplasia

DR E W NETHERTON I saw this patient in 1942, diagnosed flat warts and treated the disorder as such, without success The myeloid leukemia is probably unrelated to the cutaneous lesions However, one must keep in mind the possibility that it might have something to do with the changes around the vessels

Although I am not well informed on the histology of this disease, I know that clear cells are one of the outstanding features of epidermodysplasia These same cells are seen in flat warts I think that the changes in the epidermis are minimum

Another factor against the diagnosis is that epidermodysplasia verruciformis usually appears earlier in life As Dr Cole pointed out, the lesions are more symmetric and more extensive, and some of the lesions are usually more like keratoses All these are uniformly a flat and angular, pink, skin-colored type of lesion I think that there were some with linear distribution, all features of juvenile warts

DR G W BINKLEY After five years of observation, I began to doubt the diagnosis of verrucae planae One of the reasons is the color of the papules

The papules are reddish brown or a dull red color, much redder than common verrucae planae Verrucae planae may be yellowish brown, but these are highly colored by a persistent vasodilatation, which could be completely removed by pressure

The patient was aged 38 when lesions appeared The lesions are bilateral in distribution on the upper extremities

The biopsy specimen showed a dyskeratosis which simulated flat wart in appearance but also was consistent with epidermodysplasia

I considered the entity of Hopf which he described under the title "Acrokeratosis Verruciformis" (Hopf, G *Dermat Ztschr* 60 227, 1931)

The changes in acrokeratosis are similar from an anatomic viewpoint but differ clinically in that there are lesions on the palms The patient presented had no palmar involvement

DR H J PARKHURST May I remark that in many cases flat warts fail to disappear after treatment?

### Cutaneous Horn Presented by DR J H BARR

M C is a white woman aged 64 She had always been in good health Systemic review is noncontributory In June 1944, she noticed that her comb caught in hair behind her left ear Further observation revealed a small tumor She applied home remedies, with no effect The tumor continued to enlarge gradually during the ensuing months, and in the past month there has been a rapid growth She is well developed and well nourished

There is a large, well defined tumor mass behind the left ear, having the appearance of a horn The base measures approximately 9 by 10 cm It is soft red and vascular The remainder of the tumor mass tapers to a point approximately 8 cm above the base and is characterized by keratinization

There was no significant lymphadenopathy The Kline reaction of the serum was negative The hemogram and urinalysis gave normal results A roentgenogram of the skull showed no destruction of the bone

Biopsy of the tumor mass revealed a squamous cell papilloma with much keratinization, showing local invasion of scalp There was insufficient cellular pleomorphism to warrant a diagnosis of malignant change

The lesion was widely excised, tissues of the scalp being removed down to the galea Thiersch grafts were then taken from the left thigh and applied to the aforementioned area The area is now completely epithelized and shows no evidence of recurrence

### DISCUSSION

DR J R DRIVER Had I seen this patient, I do not believe that I should have recommended operation I do not think that there is any cutaneous horn that would assume this size without malignant degeneration at the base I should have advised use of interstitial radium needles

Excision, which was performed here, and Thiersch grafts have apparently been successful It is rather surprising to me, because with a squamous cell lesion one would expect a recurrence in the grafts One would hesitate to do skin grafting on the base of an epithelioma before being certain that there was not going to be any recurrence If the tissue which was removed has been preserved, it is possible that review might reveal something

DR H G MISKJIAN I did not find a single section that appeared malignant I think that the conception that the bases of all these cutaneous horns are malignant must be changed I have seen others that were not malignant

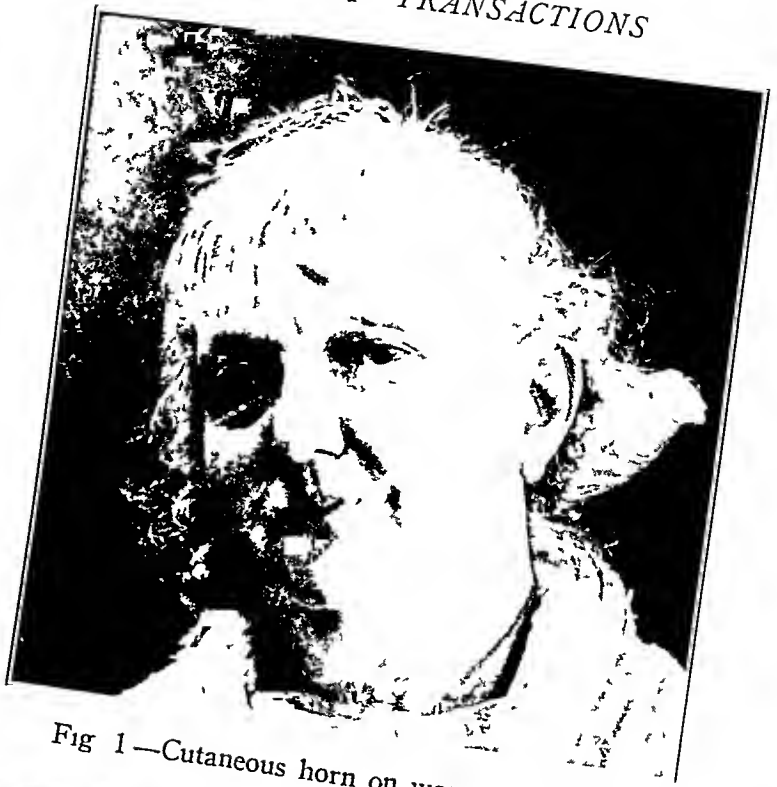


Fig 1—Cutaneous horn on woman aged 64

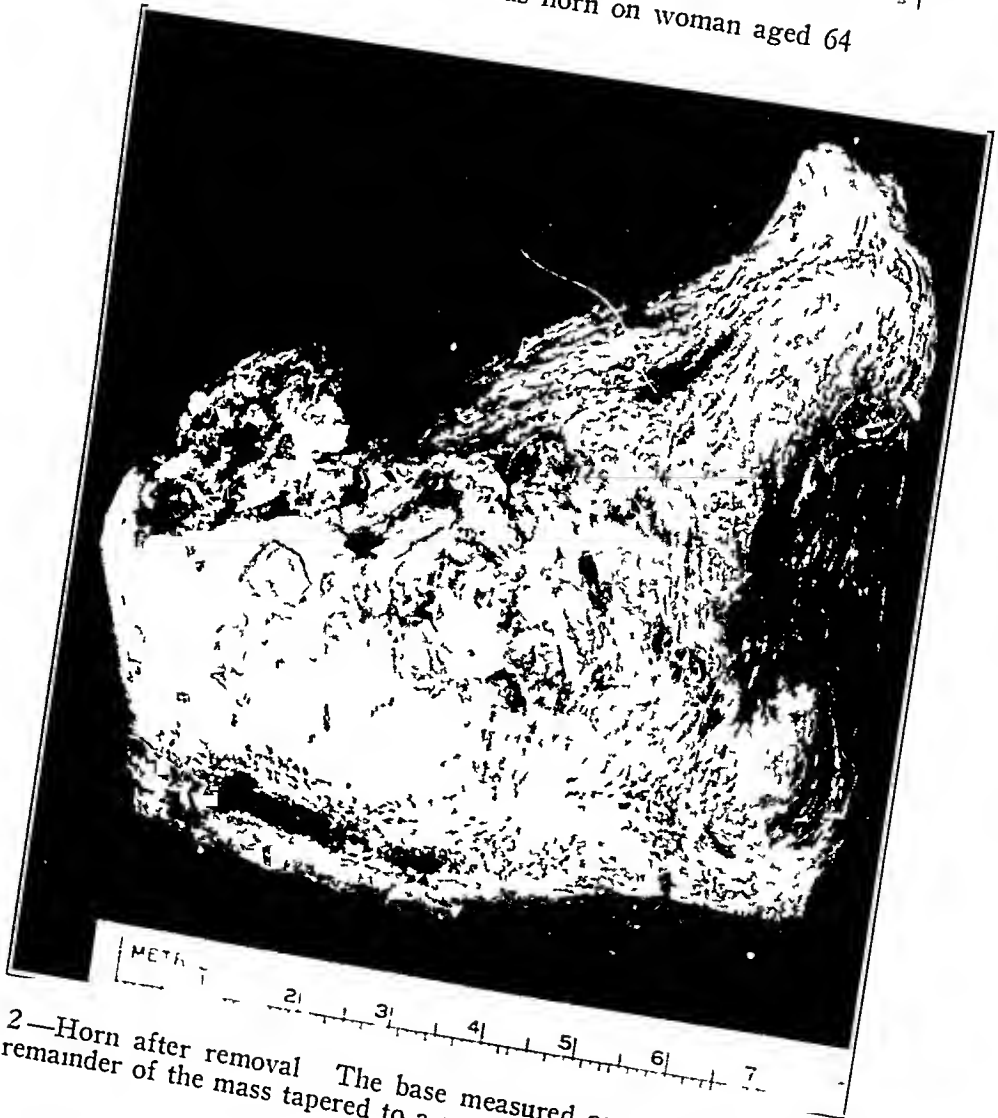


Fig 2—Horn after removal The base measured approximately 9 by 10 cm, and the remainder of the mass tapered to a point about 8 cm above the base

DR J H BARR The section was made through the base of the horn There are about fifteen slides, and they all show the same nonmalignant papilloma

**Acne Conglobata** Presented by A R SWEENEY, United States Marine Hospital No 6 (by invitation)

T E H, a white man aged 48, was a marine engineer His father died at 73 of "heart trouble" The patient's last service was in the South Pacific from September 1944 to February 1945 He has had seventeen surgical procedures, mostly incision and drainage and attempts at resection of sinus tracts about the anal and crural regions

Following a burn of the face and chest in 1923, pustular lesions appeared in the burned areas They spread to involve the back, axillas, buttocks and scrotum Since October 1944, during his service in the tropics, the lesions have been severer and more frequent

There are multiple keloids on the face, neck and scalp The skin of the face, neck, trunk and especially the perianal regions, buttocks and crural regions is involved in a scarring process with multiple purulent sinus tracts and hypertrophied tissue There is an indurated mass about the size of a large orange in the right buttock, surrounded by fibrous tissue and evaginated old surgical scars

Repeated cultures of material from sinuses showed a growth of *Staphylococcus albus* Urinalysis gave normal results The Kline reaction of the serum was negative, and the basal metabolic rate was 0 per cent

The biopsy specimen showed a pronounced verrucous hyperplasia of the epidermis with parakeratotic hyperkeratosis, acanthosis and dyskeratosis A few epithelial pearls with keratinization were in areas of acanthosis The changes were consistent with pseudoepitheliomatous hyperplasia

He has received numerous types of treatment, including local medication, autogenous vaccine, ultraviolet irradiation, repeated incision and drainage, filtered roentgen irradiation and 1,000,000 units of penicillin intramuscularly, with no improvement

#### DISCUSSION

DR H J PARKHURST The localization of multiple lesions in the axillas and perianal regions suggests that there may have been an infection of the apocrine glands which would suggest hidradenitis suppurativa, possibly, in addition to the acne conglobata

DR H N COLE This patient brings up the point that has been made by Dr Duemling and others, that men with a tendency to a severe acne—and the same would also apply to those with hidradenitis—are probably not going to do well if they reside in a hot climate When they return to this country and into a cooler climate, they seem to do better This man, who was an engineer on a ship, was sent to one of the hottest places in the world, the south coast of Persia The process immediately began to get bad and has been disabling since

**A Case for Diagnosis (Lichen Sclerosus et Atrophicus?)** Presented by DR E W NETHERTON and DR W R HUBLER

Mrs F S, a white woman aged 29, came under observation for the first time on Feb 16, 1945 The eruption which she presented at that time was limited mostly to the extremities, the lesions being more numerous on the thighs She stated that for the past year oval and annular, reddish brown lesions had appeared gradually in the aforementioned areas There were no subjective symptoms In February the eruption consisted of papules and plaques The papules were round and angular, flat, varied from the size of a matchhead to that of a split pea, smooth and brownish pink The larger lesions tended to be oval, with central scaling of a furfuraceous type, and in some of the lesions there was a suggestion of atrophy of the central portion Some of the lesions were composed of a group of the small papules On diascopic examination the lesions could not be completely obliterated

During the period of observation, which extended from February to the present, the lesions have enlarged slightly and have become smooth and of a white, ivory color. The eruption now consists of small, oval, slightly irregular, raised, white plaques and papules, some of which have a slight amount of scaling and central scarring and possibly atrophy. There are no follicular plugs.

Sections of the biopsy specimen which was taken when she was first seen showed the following changes: the surface epithelium showed a slight amount of hyperkeratosis, there was atrophy of the epidermis with absence of most of the interpapillary pegs, there was lymphocytic infiltration in the papillary and sub-papillary layers and there was a slight amount of liquefaction degeneration of the basal layer of the epidermis. The infiltration also involved the pilosebaceous follicles, the middle portion of the corium appeared to be normal.

#### DISCUSSION

DR C L CUMMER: I do not think that the type of lesion corresponds to the atrophy which has followed the involution in the cases I have had. It looks to me more like a depigmentation than it does lichen atrophicus.

I saw a bluish cast to the skin in my patients as the lesions cleared, especially in 1.

DR E W NETHERTON: The disorder in this case has been a diagnostic problem. When these lesions appeared, they were pinkish brown. Some of them today suggested it, but they were not typical. Early in the course of the disease they developed a furfuraceous shine, with a grayish color. When it was scraped slight scaling could be demonstrated. That went on, finally, to a point at which the lesions became, as they are today, white. Some of them, we thought, had atrophic scarring. There are no follicular changes.

The biopsy specimen does not show the atrophic changes that take place in that particular disease. However, the biopsy specimen was taken early, and we have been unable to take a biopsy specimen of the lesions after they have become white and waxy.

Dr Cummer said that the appearance is not that of typical lichen sclerosis. That was the reason we presented it as a case for diagnosis. There are no subjective symptoms. These lesions come gradually, a few at a time. They have been rather slow, evolving to the point where there is an ivory color, which we think is scarring or a slight atrophic change.

I think that it is more than some type of atrophy. We could not make up our minds to call it Leca's atrophic type, because I do not believe that it shows the histologic changes.

**Pseudoxanthoma Elasticum** Presented by DR E W NETHERTON and DR. W R HUBLER

In C M., an 8 year old white girl, there have developed numerous flesh-colored papules on the upper part of the trunk since August 1944. The initial lesions appeared suddenly over the sternum at that time. These lesions have not increased appreciably in size, but new solitary papules have continued to appear. All the lesions which appeared have persisted. There are no subjective symptoms.

There are two raised, flat, flesh colored nodules 5 cm in diameter over the sternum. These show the remains of small papules at their peripheries. In addition, numerous flesh-colored, smooth, flat, round and linear papules 2 to 3 mm in diameter are present on the arms and shoulders. Fine telangiectatic blood vessels course over the surface of all lesions. The papules become pink and edematous when scratched. No angioid streaks were present in the fundi.

There is no family history of a similar cutaneous disease. The patient's mother died of Addison's disease.

The hemogram was normal. The Wassermann and Kahn reactions of the serum were negative.

Histologic examination of a representative papule revealed separation and fragmentation of the bundles of collagen and moderate edema of the midcorium. A sparse perivascular lymphocytic infiltrate was also present in the corium. The epidermis was normal in appearance. Weigert elastic tissue stain revealed fragmentation of the elastic fibers in the midcorium.

#### DISCUSSION

DR H N COLE I do not think that I have ever seen pseudoxanthoma with the picture that this patient presents. These raised, firm lesions are different from those of pseudoxanthoma elasticum, which are little raised above the surface of the skin. It is only where the skin is under motion, usually around the arm or neck, that there is wrinkling of the skin so characteristic of the disease.

This is an infiltrated disease. While they do not have a tendency as yet to clear up in the center, I suggest granuloma annulare. On examination of the section of the tissue in the hematoxylin and eosin stain, there is one area in the corium that shows a localized cellular infiltrate much as is seen in granuloma annulare. There are no giant cells and no tendency to necrose in the center. Perhaps later, those changes will appear.

Moreover, on examining the section with the elastic tissue stain, I was not convinced there was enough breaking up of the elastic tissue fibers for pseudoxanthoma elasticum. Then, too, this child does not have any changes in the retinas. Of course, she is young, and, if it is pseudoxanthoma elasticum, angioid streaks may develop later.

DR E W NETHERTON I agree with Dr Cole that this is an unusual type of this disease, but I believe that it is pseudoxanthoma elasticum. When we saw this child, we did not make the diagnosis clinically. The diagnosis was made on pathologic findings, confirmed by Dr Harry Goldblatt and his associates. They think that it is histologically characteristic. That is one reason we accepted the diagnosis. The changes in the elastic tissue show decided fragmentation. It has been stated that the nodules, these large lesions, may start as papules. I believe that there are streaks commencing to develop parallel to the clavicle.

As for the histologic changes, there was practically no infiltrate except the one area Dr Cole mentioned, but throughout the section there were fragmentation and edema. There was little cellular infiltrate in many sections taken out of one lesion that was about the size of the smallest papule and the largest on the chest. One would expect more inflammatory changes in some of these sections. The fragmentation of the elastic tissue I thought was severe and, for that reason, I think that we can accept the diagnosis.

#### Reticuloendotheliosis (Mycosis Fungoides?) Presented by DR E W NETHERTON and DR W R HUBLER

Mrs A R, a white woman aged 50, was first seen at the Cleveland Clinic June 10, 1944, with a generalized, pruritic, vesicular and bullous eruption of one week's duration. She stated that she had had an erythematous eruption periodically for five years, which had partially cleared with roentgen ray treatment. She had taken no medicine and had not used local applications at the onset of the present eruption, but just prior to coming to the clinic she had received three intravenous injections of an unknown medicament and several roentgen ray treatments from her local physician, with no improvement. She was hospitalized. The eruption subsided with bland external treatment and hypodermic injections of sodium arsenate. A clinical diagnosis of dermatitis herpetiformis was made at this time. Two months later a generalized erythroderma was noted. This too was pruritic.

The eruption for which she is presented is similar to the initial eruption which she had several years ago. It consists of well defined, red, slightly raised, infiltrated, rounded and gyrate, slightly scaling plaques. The eruption is limited to the trunk and upper portion of the extremities. Numerous islands of normal skin

are surrounded by the erythematous plaques. No other abnormal findings were disclosed by physical examination.

Repeated hemograms in 1944 were normal, except for occasional abnormal lymphocytes. On July 9, 1944 the leukocytes numbered 4,650 cells per cubic millimeter, and the differential count showed 72 per cent neutrophils, 18 per cent lymphocytes, 1 per cent eosinophils and 8 per cent monocytes. There were no abnormal forms. The hemoglobin content was 78 per cent (12 Gm), and there were 5,300,000 erythrocytes. The blood sugar level was normal. The total plasma protein content (Tiselius' method) was 5.72 Gm per hundred cubic centimeters. The albumin content was slightly diminished (2.92 Gm per cubic centimeter).

Sternal puncture was performed. A normal histologic picture was reported.

Histologic examination of a portion of a plaque from the right thigh showed a sharply limited, dense, cellular infiltrate in the papillary and subpapillary corium, which extended into the epidermis in some portions of the section, with the production of liquefaction degeneration. The infiltrate was composed of closely massed cells with scant vacuolated cytoplasm and large distorted nuclei with wrinkled nuclear membranes and a fine, basophilic internal pattern. Many had moderately enlarged nucleoli. An occasional mitosis was present. In some areas slender, collagenous bundles were present between the cells. Wilder stains showed a rich network of moderately coarse argyrophilic fibers in the region occupied by the previously described lesion. There was intimal hyperplasia of some of the deeper blood vessels. Pigment was present in some of the areas of infiltrate.

#### DISCUSSION

DR J. R. DRIVER: I think that the definite infiltration of these lesions suggests mycosis fungoides.

The process has been pruritic in the past, which would go with that disease. I do not think that it is a typical mycosis fungoides, but it looks more like that than anything else.

DR W. R. HUBLER: When we saw this case, we felt that clinically it was typical of mycosis fungoides. However, on histologic examination, the cellular infiltrate is of such a uniform type that we felt that it did not fit with that picture at present, and the diagnosis of endotheliosis instead of mycosis, as suggested by Dr Goldblatt, was accepted.

It is true that a good many of these conditions eventually turn into mycosis fungoides or one of the lymphoblastomas or sarcomas. It may be that in six months or a year we will change the diagnosis from reticuloendotheliosis.

I do not believe that the entity of reticuloendotheliosis is a clearly defined group. I feel, from the few cases I have studied and read about, that they usually develop into one or the other of the lymphoblastomas, so I can agree with Dr Driver's suggestion of mycosis fungoides, at least as far as the future is concerned.

#### Superficial Epithelioma of Bowenoid Type. Presented by DR SAMUEL AYRES III, DR TOMAS GENATIOS and DR WOODROW W. MURPHY

M. P., a white man aged 70, is presented from the Department of Dermatology and Syphilology, Cleveland City Hospital, service of Dr Cole and Dr Driver. He had a persistent lesion of the left foot of ten years' duration.

On the dorsum of the left foot is a tender, irregular, slightly raised, ovoid lesion, 6 by 3 cm in diameter, having a slightly moist, smooth, erythematous surface with white scales. Along one border are several confluent papules.

The Kline reaction of the blood was negative. The histologic examination showed acanthosis and parakeratosis. The basal layer of rete cells was sharply defined, and there was no evidence of invasion of the corium. There were many abnormal cells within the epidermis, some of which were multinucleated. The cells were large, and many showed disturbed polarity. Their nuclei showed variability of size, shape and chromatic content. There was a slight infiltration of lymphocytes in the superficial layer of the corium.

## DISCUSSION

DR ROY L. KILE (by invitation) When I first saw this lesion there was only an area of infiltration. I thought that it was irritation from his shoe, although it had lasted a long time. The resident prescribed soothing local application. After a biopsy was made, it was surprising to find that it was a superficial epithelioma. I think that one end of the lesion has become slightly verrucous in the last few months.

It has been my experience that this type of lesion does not usually respond to irradiation.

DR J. R. DRIVER This is a rare disease, and it is not seen often. I thought that it might respond to irradiation. Since that biopsy specimen was taken, about a year ago, the lesion has developed a papillomatous hyperplasia. A biopsy specimen now might show some penetration into the corium. It would be interesting to have a repeat biopsy specimen from the lower portion, then treatment would depend on what that biopsy specimen showed.

DR W. R. HUBLER Dr. Netherton and I have had the opportunity of seeing a number of cases that were somewhat similar and were histologically identical with this one. They responded well to superficial roentgen rays given with the Phillips x-ray therapy machine, which has a low kilovoltage and short target-skin distance. These lesions received 4,000 or 5,000 r.

DR H. J. PARKHURST Since there is some question as to the value of irradiation in this case, I should favor a thorough destruction with electrocoagulation.

**Pinta** Presented by DR SAMUEL AYRES III, DR TOMAS GENATOS and DR. WOODROW W. MURPHY

W. T., a Negro man aged 55, is presented from the Department of Dermatology and Syphilology, Cleveland City Hospital, service of Dr. Cole and Dr. Driver. He complains of an eruption which began in 1926 with scaling of the palms, spreading to the dorsa of the hands and then to the flexor surface of the wrists, with hyperpigmentation, followed by depigmentation of a portion of the wrists. One year ago similar lesions developed on the thighs and legs.

He had a lesion on the prepuce in 1910, diagnosed as "chancroid" and treated only by circumcision. He was found to have a positive serologic reaction for syphilis in 1937 and received sixteen intramuscular and sixteen intravenous injections, at which time the eruption improved. No further therapy was given until November 1944, when the Kline and Kahn reactions of the blood were found to be positive. He received ten injections of oxophenarsine hydrochloride and one of bismuth subsalicylate. The eruption on the lower extremities, which was scaly, improved decidedly, according to the patient.

He was born in Tennessee, but since his youth he has spent most of his time in northern United States. He had never been outside the United States.

There is a slate gray, slightly scaly eruption with irregular, sharply defined borders present on the flexor surfaces of the forearms and the extensor surfaces of the legs and thighs, with discrete scattered lesions over the abdomen. On the flexor surface of both wrists are sharply defined, irregular areas of depigmentation. There are no sensory changes. There is some atrophy over the tibias. Small posterior cervical epitrochlear and inguinal lymph nodes are palpable. There is an aortic systolic and diastolic murmur.

The serologic reactions were

	Wassermann	Kline Diagnostic	Kline Exclusion
November 1944	Not done	++	+++
February 1945	Negative	+	++
May 1945	Negative	++	++

The examination of the spinal fluid gave normal results. A differential count of the blood cells showed 5 per cent eosinophils. A roentgenogram of the chest

and cardiac fluoroscopy showed nothing abnormal. Repeated dark field examinations of the border of a hyperpigmented lesion revealed no spirochetes.

Histologic examination of a similar hyperpigmented area showed hyperkeratosis, a pigmented basal cell layer and large amounts of intracellular and extracellular pigment in the upper cutis. There was no evidence of inflammation.

#### DISCUSSION

DR G. W. BINKLEY: I think that this is pinta. The man had spirochetosis, because there have been positive Kline exclusion and diagnostic reactions for many years. He had been treated with arsenicals and heavy metals. After such treatment the serologic reactions are weak, but there is a sufficiently high titer to make a diagnosis of spirochetosis even now.

Pardo-Castello and Ferrer, on pinta (*ARCH DERMAT & SYPH* 45:843 [May] 1942), stated that treated patients with pinta tended to be seropersistent, just as old syphilis is seropersistent when treatment is started late. "The Wassermann and Kahn reactions remain positive in many cases, in spite of the most intensive and prolonged treatment. In others, the reactions recede slowly and finally become negative."

In a case from University Hospitals which was presented before the Central States Dermatological Society (*ARCH DERMAT & SYPH* 52:415, 1945), the possibility of pinta was not thought of until after antispirochetal therapy was given, so a golden opportunity to prove pinta was lost. A proof of pinta as differentiated from syphilis is to take an old lesion like that on the forearm, draw serum and find the organism. The characteristic of *Treponema carateum*, or the pinta spirochete, is that it is supposed to be present in the skin as long as twenty or thirty years after infection takes place. Otherwise, there is no way to differentiate a pinta spirochetosis from syphilis. At present, the differential diagnosis must be made clinically.

From the dermatologic viewpoint, I have regarded these cases (the one presented today and the one presented before the Central States Dermatological Society) as pinta because the host's reaction to the spirochete differs entirely from late cutaneous syphilis as it has been known in the past. In a high per cent of late cutaneous pinta, persistent erythematous areas are present on the forearms and on the extensor surfaces of the legs. The erythema has a sharp border. The lesions remain red for years and develop hyperpigmentation, and finally areas of vitiligo appear. After antispirochetal therapy the erythema slowly fades, but the outline of the area can still be seen.

Perhaps some of you may have been impressed by the photograph of the Negro woman with extensive vitiligo (Fox, H. *ARCH DERMAT & SYPH.* 40:433 [Sept] 1939). Vitiligo is variable and is often minimal. In *Corpus Iconum Morborum Cutaneorum* (Nékám, L. *Corpus Iconum Morborum Cutaneorum*, Leipzig, Johann Ambrosius Barth, 1938, vol. 2, pp. 250-251), there are illustrated cases of pinta, with only a small triangular area of vitiligo on the flexor surface of the wrist such as this man has.

In addition to the vitiligo on the flexor surfaces of the wrists, this man has had the persistent erythema of his palms with hyperkeratosis. In the cases I have seen in Cleveland and in those which Leiberthal described in Chicago, it is usually present.

DR J. E. RAUSCHKOLB: Dr. Tomas Genatios has pointed out that the history of this case goes back something like twenty-five years. During World War I, the patient was stationed throughout his Army duty at Fort Sheridan here in the states. He has never been out of the United States. He was discovered to have a positive Wassermann reaction shortly after the war and was treated. He might be one of the patients whose condition Leiberthal called pinta, for he came here from Chicago. Dr. Genatios thinks that this is a typical case of pinta.

When there were symmetric depigmentation and hypertrophic, increased pigmented, almost granular lesions at the peripheral border involving the lower extremities, that is, the medial extremities, he would diagnose pinta.

We did not find *Treponema carateum*. That is not always possible, although we should like to find it either in tissue section or by dark field search. The Kline test still elicits a positive reaction after twenty-five years' duration, so it can be regarded as a serologic-fast type of chronic syphilis or syphiloid or pintid type of *Spirochaeta* infection.

I traveled in Mexico searching for cases of pinta. There are supposed to be many cases of pinta in Mexico, but I found only 1 that was a counterpart of this

### **Papulopustular Verrucous Sporotrichosis Simulating Blastomycosis** Presented by DR E W NETHERTON and DR W R HUBLER

C M, a white man aged 49, dates the onset of his present eruption about Dec 10, 1944. At that time he pulled a couple of slightly infected hairs from the right nostril. In a few days the nose became red, swollen and tender. There was no itching. He consulted his physician, who prescribed sulfathiazole ointment for external use and sulfathiazole by mouth. Within a short time a generalized eruption developed necessitating the withdrawal of the use of the sulfonamide drug. The nose became larger. Small pustules developed on the surface of the distal portion of the nose, and later small papulopustules developed on the right side of the face, below the eye. The lesions on the face were acneform in type. There were no large, nodular lesions. He is a greenhouse employee and just prior to the onset of the eruption was working with mushrooms.

When this patient was seen for the first time, on March 28, 1945, there was a papulopustular, verrucous, crusted lesion involving the tip of the nose and extending upward to involve about two thirds of the nose. There were acneform lesions on the right side of the face, near the nasolabial fold and below the right eye. There was a small, soft, cystic lesion on the side of the nose, near the inner canthus of the right eye. The most intense reaction involved the tip of the nose, where the surface of the nose was verrucous and crusted. The lesion was not sharply demarcated, however, and there were many small, pinpoint pustules at the periphery of the lesion. The eruption has improved materially under treatment.

The acneform lesions have disappeared, leaving pink, slightly depressed scars. The tip of the nose is still erythematous, somewhat thickened and covered with a gray seborrheic scale. Pustules are not present now.

A section of the biopsy specimen which was examined March 29, 1945, showed some acanthosis and some liquefaction of the basal layer. In the papillary and subpapillary layers and upper portion of the corium there were numerous lymphocytes, large mononuclear cells, a few neutrophilic leukocytes and also a few plasma cells. A diagnosis of chronic granulomatous inflammation was made.

Cultures made March 28, 1945, showed a growth of *Sporotrichum Schenckii*. The identification of the organism was confirmed by Dr Morris Moore, of the Barnard Free Skin and Cancer Hospital, in St Louis. Wassermann and Kahn reactions of the serum were negative.

Treatment was use of saturated solution of potassium iodide N F by mouth and three roentgen ray treatments of 75 r each. He is taking 35 Gm of potassium iodide after each meal.

### DISCUSSION

DR ROY L KILE (by invitation). This case of sporotrichosis is different from either the localized lymphangitic or the generalized subcutaneous type. The former is usually caused by *S. Schenckii* and the latter by *Sporotrichum beurmanni*. Both usually respond rather promptly to therapy. This patient is also responding rapidly. The lesions are much more verrucous than those usually seen, and the location on the face is unusual. They are syphiloid in type and have ulcerated. One could not have made a diagnosis in this case without finding the fungus.

DR E W NETHERTON. The features of this infection are the verrucous changes, the location and the fact that it does not fall into the customary nodular or gummatous type of sporotrichosis. The small pustules remotely simulated

blastomycosis The lesions were sharply demarcated and had the distinct borders found in blastomycosis

Papular sporotrichosis has been described recently by Costa and Junqueira (ARCH DERMAT & SYPH 51 261 [April] 1945) They reported a case of papular sporotrichosis with lesions on the nose I recall reading reports a few years ago of sporotrichosis with lesions of this type on the hand

**Acanthosis Nigricans** Presented by DR B LEVINE.

A G is a white boy aged 16 A cousin of this patient has a similar eruption Symptoms began a little over three years ago with increased pigmentation of the axillas and the groin The patient has always been tall and obese. He is 6 feet  $1\frac{1}{2}$  inches (186.6 cm) tall There are areas of hyperpigmentation in both axillas, the neck, the groin, the inner surfaces of the thighs and the flexor surfaces of the elbows In the pigmented areas, the skin is thickened with papillary hypertrophy, thus accentuating the lines of cleavage of the skin The crests of the papillae are deeply pigmented, whereas the crevices show no pigmentation There is no pruritus

A culture of material from the axilla showed *Staphylococcus albus* and a type of *Penicillium* as a contaminant

Histologic study of a section of skin showed the epidermis about average in thickness, with alteration of the epidermal cells The upper layers showed considerable dyskeratosis, and there was an abundant layer of cornified cells covering the surface and filling numerous crypts which occur between interpapillary projections The crypts are apparently unrelated to sweat glands or hair follicles There was an increase in brown, granular pigment in the basal layer of cells The corium was thickened by collagenous fibers and showed diminution in the number of sweat glands and hair follicles and increase in the number of capillaries, with moderate pericapillary round cell infiltration In places there was increase in fibrous tissue about capillaries

#### DISCUSSION

DR H J PARKHURST This boy has gained 100 pounds (45.4 Kg) in weight over a three year period, and atrophic striae of the arms and trunk, as well as hyperpigmentation of the axillas, have developed I feel that this may be a case of pituitary basophilism

DR H N COLE I was inclined first to accept the diagnosis of juvenile acanthosis nigricans However, he certainly has the build that would go well with pituitary basophilism

DR J R DRIVER In view of what Dr Parkhurst has said, it might be worth while to have an endocrinologist examine the patient for a possible pituitary disturbance

DR B LEVINE I do not think that it is pituitary basophilism I do not know how else to classify this except as acanthosis nigricans I did this for these reasons There was papillary hypertrophy in the hyperpigmented areas, and the distribution of the pigment fitted typically with the description of the juvenile type of acanthosis nigricans The ridges of the verrucous areas are pigmented, but the valleys lack pigment An endocrinologist has studied the patient and found no endocrine dyscrasia

**A Case for Diagnosis (Quinacrine Hydrochloride Dermatitis).** Presented by DR H G MISKJIAN

W W, a white man aged 31 years, stated that in July 1944 there developed a pruritic eruption on the upper part of the thorax while he was serving with the armed forces in New Guinea He had been taking quinacrine hydrochloride (atabrine) daily since March 1944 The eruption gradually spread to involve the face, hands and feet In December 1944, administration of quinacrine hydrochloride was discontinued, and the patient was evacuated to the United States En route

the eruption improved and has slowly regressed. The result of a biopsy performed after arrival was reported as lupus erythematosus.

Over the upper part of the chest and shoulders is a diffuse, mottled, erythematous and pigmented eruption with many tiny telangiectases and some areas suggestive of atrophy. On the occiput is an area of alopecia 3 by 2 cm. The scalp in this area is red and slightly depressed. The palms are thickened and have a mottled red color. On the right instep is a linear, red, scaly lesion with many fine telangiectases on its surface. There is a small keloid above the right breast, the site from which the previous cutaneous biopsy specimen was taken.

#### DISCUSSION

**DR H. HECHT** He has lesions on his feet that look like keratoses. I thought that the dermatitis was similar to arsenical dermatitis, so I asked him, "Did you take some pills or some tablets?" He said, "Yes, I was taking quinacrine hydrochloride." Since it improved after the use of quinacrine hydrochloride was discontinued, I think that it could be dermatitis due to quinacrine hydrochloride.

**DR H. J. PARKHURST** The erythematous patches on the extremities, scalp and upper eyelids, coming on rather suddenly as they did and fading out as they have, with atrophy remaining, suggests to me the possibility that this might have been a case of subacute disseminated lupus erythematosus.

**DR E. C. STERN** The lesions were not pruritic, and the atrophy, particularly on his neck and feet, suggests lupus erythematosus.

**DR H. N. COLE** I think that this man belongs in the group in whom this eruption has developed after they have taken quinacrine hydrochloride. It often looks like lichen planus, and in certain cases there may be some atrophy and a great deal of pruritus. There is much discussion about it yet, but probably it is secondary to the ingestion of quinacrine hydrochloride.

If they are unfortunate enough to get the combination which the boys call "jungle rot" (a bad term, which should not be perpetuated), which is a mycotic infection of the hands and feet, that completes the picture.

**DR H. G. MISKJIAN** The condition of this man has changed since the first examination. My first impression was that the eruption was a typical poikiloderma on the neck and the upper portion of the chest. There was diffuse redness and a peculiar mottled appearance. At the present time all that has disappeared. He has improved a great deal during the two months I have been able to observe him.

In this case, also, as in others, a diagnosis of lichen planus and of lupus erythematosus had been made, one by a well qualified dermatologist and the other by a man just as competent. To differentiate between the two, a biopsy was performed, but it did not lead to any definite conclusion. I do not have a report of the biopsy. There is a keloid on his chest, so I did not take another one.

First, in regard to lichen planus, I shall say that when I first saw this man there were definite papules on the wrist and anterior surface of the forearms, but a detailed examination of these papules made it obvious that it was not lichen planus. The papules had none of the features of lichen planus, such as the distinctive porcelain surface and similar aspects.

In regard to the diagnosis of lupus erythematosus, I think that it must have been suggested by the fact that the patient has a patch of alopecia on the occiput. That patch does not look like lupus erythematosus. It is a simple alopecia areata with a little redness, a slight depression and the ivory smooth texture of the skin. I do not think that there is any support for the diagnosis of lupus erythematosus because of the alopecia. It seems reasonable to incriminate quinacrine hydrochloride because poikiloderma-like lesions have been known to occur in other drug eruptions. In this case, if I am not mistaken, the patient began to take quinacrine hydrochloride in March, and his eruption developed in July. This would fit in well with the course of a drug eruption.

L. L. Praver, M D , *President*

G. W. Binkley, M D , *Secretary*

Sept 27, 1945

A Case for Diagnosis (Lymphoblastoma?). Presented by DR. WOODROW W MURPHY and DR BURT HELD

D R, a 50 year old Negro man, complains of multiple soft tumors of the scalp of twenty-six years' duration. / In 1919 he suffered from moderate pruritus of the scalp associated with the loss of scalp hair. About six months after the onset of pruritus, he noticed multiple papules in the pruritic areas. Slowly during a period of years these enlarged to form small nodules and plaques.

In 1922 the patient noticed a painless penile lesion, which healed in one month. At that time he received six intravenous injections. In 1941 the Kline and Wassermann reactions of the serum were found to be strongly positive, and he received a small amount of antisyphilitic therapy. Since April 1945 he has been treated with ten injections of 60 mg each of oxophenarsine hydrochloride and ten injections of 130 mg each of bismuth subsalicylate.

In December 1944 he was subjected to a subtotal gastric resection for a poorly differentiated adenocarcinoma with metastasis to the regional lymph nodes. Since the operation he has felt well, and no metastases have been demonstrable.

Examination of the skin reveals multiple soft, sharply defined, flat, skin-colored papules and nodules involving the temporal, parietal and frontal areas of the scalp and the periorbital areas of the face. In each parietal area the lesions have become confluent to form larger sharply defined, irregular, plaques, which show some atrophy of the overlying skin, with some loss of pigment. They are devoid of hair. These plaques are traversed by regular straight grooves that appear to be an accentuation of the normal lines of the skin and divide the plaques into multiple segments. The largest of these plaques is about 6 cm in its largest dimension and is elevated about 5 mm above the level of the skin. Examination of the lymph nodes reveals a few soft, bean-sized nodes in the inguinal, axillary and submandibular areas.

Roentgenograms of the chest showed no evidence of pulmonary infiltration. The hemogram and urinalysis showed normal conditions.

Histologic examination showed negroid skin. The epidermis showed no change of note. The corium showed a decided infiltration of cells of various types. The infiltration spared the papillary layer of the corium. The cells were seen in dense masses which had no relationship to blood vessels in the upper corium. In the deeper corium there was a moderate tendency for perivascular distribution. The commonest type of cell was fusiform to polyhedral with fibrillar processes and appeared to be related to the fixed tissues. The nuclei were oval to round and varied in amount of chromatin. Some of the cells were vesicular. Mitoses could be found after careful search. In some places, there were multiple nuclei in the cells, which nuclei tended to overlap. This differed from the ordinary Sternberg-Reed cell, however, in that those cells had more cytoplasmic processes. In addition to that type of cell, there were lymphocytes and eosinophils. Blood vessels showed decided proliferation, with obliteration of the lumen in some. Change in the blood vessels was greatest where the cellular infiltration was greatest.

#### DISCUSSION

DR DON R PRINTZ. Although the histologic changes of the disease varies, there is an infiltrate high up which suggests the possibility of a sarcoid. I thought of the Spiegler-Fendt type of sarcoid.

DR C L CUMMER. I should like to ask the presenter whether he does not think that the diagnosis of lymphoblastoma is not inconsistent with the long duration, the twenty-five years the patient claims that he has had it.

DR WOODROW W MURPHY That is correct That is a rather long duration for lymphoblastoma Lymphoblastoma was proposed because of the peculiar infiltrate, and the size suggested the possibility of mycosis fungoides We welcome suggestions as to the diagnosis and as to therapy

DR E W NETHERTON I agree that Dr Cummer's point of the duration of the lesion is against lymphoblastoma I thought that it was a sarcoid Histologically, there is confusion There is considerable fixed tissue reaction with the lymphocytes The cellular infiltrate is localized in islands and nodular types separated by dense fibrous tissue This would favor sarcoid, yet I do not think that it is histologically a sarcoid effect I do not know just where to place it I am trying to correlate the two findings and the histologic structure of sarcoid of some type

DR H N COLE It would seem that this process might come under the heading of sarcoid It is true that the man has no osseous changes, and I understand that roentgenograms of the chest show no evidence of sarcoidosis, but the histologic picture would go well with sarcoid There are cellular masses with septums of connective tissue between them I do not think that this process is deep enough for a Spiegler-Fendt type of sarcoid That is supposed to be more in the subcutis, while this is definitely in the upper corium If tuberculin tests have not been made I suggest that this be done He might have an anergy, which would help in the diagnosis

DR E W NETHERTON Was the biopsy specimen taken from one of the earlier lesions?

DR WOODROW W MURPHY It was taken from an older, large lesion at the hair line

DR J R DRIVER Have any of the lesions developed in the last year?

DR WOODROW W MURPHY No

DR J R DRIVER In talking with him, I got the impression that the disease has been much the way it is now for a number of years

DR WOODROW W MURPHY That is true The history we obtained was that of no recent lesions They have remained stationary for a number of years

**Psoriasis, Arsenical Pigmentation and Keratoses, Squamous Cell Epithelioma of the Finger with Metastasis to the Axillary Lymph Nodes**  
Presented by DR WOODROW W MURPHY and DR BURT HELD

W M, white man aged 49, entered City Hospital because of a fungating tumor of the finger In 1940 a physician prescribed potassium arsenite for psoriasis Since that time the patient has been obtaining the drug from a pharmacy without a prescription, and at the time of admission he was taking 45 drops a day In 1942 the patient noticed hard, wartlike lesions on the hands and feet In 1944, eight months prior to admission, he injured one of these lesions on the little finger on the right hand, and subsequently an enlarging fungating tumor developed

Examination reveals a generalized grayish brown pigmentation of the skin, mottled with 2 to 4 mm round areas of normal-colored skin The pigmentation is greatest over the lower portions of the abdomen and back, the axillas, the cubital fossae and the pubic areas The soles are covered with yellow hyperkeratotic papules and plaques varying from a few millimeters to several centimeters in diameter, which have developed since the destruction of similar lesions with the cautery in June 1945 The hands are covered with many hyperkeratotic papules varying from 1 to 5 mm in diameter There is a recent draining incision in the right axilla, made for a block dissection of the axillary lymph nodes

The hemogram and urine were normal The Kline and Wassermann reactions of the serum were negative The urea nitrogen and sugar levels of the blood were normal Roentgenograms of the chest were normal

Histologic examination of the tumor of the finger showed large polygonal tumor cells of squamous cell type arranged in large sheets, with some tendency at the periphery to palisading. Whorls of tumor cells with pearl formation were present. Mitoses were moderate in number. No intravascular tumor was demonstrable. Histologic examination of a keratotic lesion showed hyperkeratosis and acanthosis of skin. Histologic examination of a section of pigmented skin showed melanotic pigmentation of the superficial corium. Histologic examination of a right axillary lymph node revealed a portion of a lymph node which was replaced by stratified squamous epithelial cells growing in compact masses. There were finger-like projections from the tumor cells. Four to five mitotic figures were present per high power field.

## DISCUSSION

DR R E BARNEY This patient illustrates the danger of the prescription of arsenic for chronic diseases of the skin. This has been seen before repeatedly. I believe that Dr Netherton stated about two years ago, when I showed a patient with the same symptoms, that he never uses arsenic for psoriasis.

DR L L PRAVER In a previous discussion Dr Ormsby was quoted on the value of tablets of arsenic trioxide over potassium arsenite. Tablets of arsenic trioxide are not supposed to produce this type of reaction.

DR H N COLE When patients are given a prescription for potassium arsenite and the druggist says, "Oh yes, potassium arsenite," then patients learn the name. The patient immediately follows that up and asks for potassium arsenite over the counter, and it is sold occasionally. If one prescribes liquor acidi arseniosi U S P., it is not easy to remember and to repeat.

Lichen Planus with Involvement of the Palms Presented by DR WOODROW W MURPHY and DR BURT HELD

M B, a white man aged 73, complains of pruritic lesions of the hands, feet, axillas and groins of five months' duration. Lesions were first noticed on the hands and were associated with severe pruritus. In about six weeks the palms had become covered with lesions and new ones appeared on the dorsa of the hands, the ankles, axillas and groins. When first seen, the palms of the hands were covered with many, hard, 3 to 4 mm, yellowish white, umbilicated, globular, flat-topped papules. He was treated with three weekly injections of 130 mg of bismuth subsalicylate. The last injection was given Sept 6, 1945.

Examination reveals the palms to be erythematous and also to be covered with many close, 2 to 3 mm, yellowish white, slightly elevated flat papules. Scattered around the borders of the fingers and palms are 3 to 5 mm, yellowish white, umbilicated, flat-topped papules covered with a thin translucent scale. On the dorsa of the feet and hands and on the wrists are typical violaceous, angular, flat-topped papules, some of which are arranged in a linear fashion. In the axillary region and groins are multiple discrete linear, flat-topped, violaceous, pruritic plaques averaging approximately 2 cm in diameter. On the right buccal mucosa there is a slightly erythematous lesion covered with fine retiform bluish white lines 3 cm in diameter. An anterior segment has been removed for histologic examination.

The Kline and Wassermann reactions of the serum were negative. The hemogram and urine were normal. A roentgenogram of the chest was normal.

Histologic examination of a papule from the wrist showed moderate hyperkeratosis. The epidermis was hyperplastic in one area, and below it was a superficial dense lymphocytic infiltration. There was moderate edema in the papillary and subpapillary layer. Capillaries and histiocytes were more numerous than usual.

Histologic examination of a papule from the palm revealed hyperkeratosis, which, the site of the lesion being considered, was normal. There was no acanthosis. There was separation of the epidermis from the papillary corium in places. There was a moderate superficial lymphocytic infiltration.

Histologic examination of the lesion from the right buccal mucosa revealed a specimen which appeared to be cut obliquely to the surface, giving the mucosa unusual breadth. Keratinization was slight. There was an infiltration of lymphocytes limited to a narrow zone just beneath the epithelium.

## DISCUSSION

DR E C STERN Six months ago I saw a girl with lichen planus. Later her father came with lichen planus on his hand, the same disease. It spread to his entire skin. I do not know whether there is any connection between the 2 cases. The daughter was cured in three or four months.

DR L L PRAVER If this man becomes resistant to bismuth therapy and other treatment, I suggest the use of vitamin A. Dr Obermeyer presented a case before the Los Angeles Dermatological Society in which hypertrophic areas responded to large oral doses of vitamin A.

DR J R DRIVER Several years ago Dr Cole and I saw a patient with extensive lichen planus involving the mouth. He also had lichen planus of the palms. The eruption cleared up after a few months of treatment. His sister came in several years later with the same disease. I wonder if others have seen such cases when there are more than one in the same family.

DR J E FISHER Recently I had 2 sisters with lichen planus under my care. They gave a history of the appearance of lesions after their mother died.

**Larva Migrans** Presented by DR DON R PRINTZ for DR H N COLE and DR J R DRIVER

B F, a white man aged 55, was first seen on Sept 12, 1945, complaining of an eruption on the right calf which started as a red pimple that itched intensely. The patient had been in Florida in June 1945, and it was soon after this that the pimple appeared, but not until four weeks ago did it start to spread. There was some tenderness and at times pain.

Examination shows a fine pencil-like lesion on the right calf that extends in a gyrate pattern. The lesion is slightly elevated above the surrounding surface and has the appearance of containing vesicles along its course. One might compare the lesion to the trail left by a burrowing ground mole. There are some redness and edema along the course of the eruption. There are also three crusted areas, which have been painted with gentian violet medicinal. These are the results of ethyl chloride spray applied to the lesions.

Treatment has been three intramuscular injections of small doses of fuadin.

## DISCUSSION

DR DON R PRINTZ Dr D C Smith, of the University of Virginia, published an article several years ago in *The Journal of the American Medical Association* (123:694 [Nov 13] 1943) about the use of antimony preparations in larvae and similar infections. Dr Wilson of Jacksonville, Fla., started to use fuadin in creeping eruption. His first dose was 5 cc daily for five days, but he found out by gradually reducing the dose that that amount was not necessary. He reduced the dose to 5 cc repeated in one week, and his results were still good. In only 1 patient out of 10 that he treated did he have any trouble, and in children up to 8 years old only 1 cc was required (Wilson, J F. Treatment of Creeping Eruption with Fuadin, J Florida M A 30:425, 1944). In this case we injected only 1 cc, and the larva was dormant for five days. Previous to that, it had been moving every day. If 1 cc would do that, probably 5 cc would be lethal.

DR J E FISHER In addition to fuadin what other type of treatment is effective?

DR H N COLE In the past, therapy has been freezing with either ethyl chloride or solid carbon dioxide. If one is lucky enough to catch the place where the larva is, that will take care of it. One may or may not get the right place. The result does not show up for some time. The family physician had seen this

patient, made the correct diagnosis and treated him with ethyl chloride but did not freeze the larva

**Dermatosis, Progressive Pigmentary.** Presented by DR DON R PRINTZ for DR H N COLE and DR J R DRIVER

B G, a white woman aged 19, was seen on Sept 6, 1944, complaining of brown spots on her legs, of about two years' duration, which had appeared after she had received a bruise on the right leg. The lesions have increased in number and progressed downward. The same lesions are appearing on the left leg. She states that she has a tendency to bruise easily.

Examination reveals small, discrete, burnt orange-colored lesions with irregular borders, some of which are confluent. They are distributed over the lower anterior and lateral aspects of the right leg. Similar lesions are to be found in the region of the left ankle. The lesions blanch a little under pressure, and there is no follicular involvement. No signs of hemorrhagic diathesis are present. Physical examination otherwise gives essentially normal results.

The hemogram and urine were normal. Kline diagnostic and exclusion tests of the serum elicited negative reactions. The prothrombin level was 82 per cent of normal, and a repeated test, two days later, was 75 per cent of normal by Quick's method. Bleeding time was one minute and fifty-five seconds and clotting time three minutes and fifty seconds. The blood urea nitrogen level was 12 mg per hundred cubic centimeters, urea clearance was normal. The Rumpel-Leede test gave essentially normal results.

Histologic examination of skin from the leg revealed considerable hyperkeratosis with some thickening of the stratum mucosa. In the upper portion of the dermis were large mononuclear cells and some lymphocytes. There were also scattered erythrocytes and phagocytes containing granular light brown pigment in the upper dermis. Sections treated with hydrochloric acid and potassium ferrocyanide showed a large amount of iron-containing pigment in the dermis.

#### DISCUSSION

DR H G MISKJIAN: This might be called cutaneous hemosiderosis, a limited type. Such conditions have been proved to be of capillary origin, as can be seen clinically. They should be called a type of capillaritis. In fact, if there is any pure type of this, the histologic structure of progressive pigmentary dermatosis shows it. These capillary changes bring the disease into the large group of cutaneous disease due to capillaritis.

**Myoblastoma** Presented by DR DON R PRINTZ for DR H N COLE and DR J R DRIVER

N M, a white man aged 71, was seen first on April 10, 1945, complaining of a white spot on the tongue, of about three weeks' duration, which rubbed against his teeth and became slightly tender after he smoked his pipe.

Examination revealed a small, dull white, indurated lesion, 6 mm in diameter, on the left side of the tongue, slightly toward the ventral aspect, 3 cm from the tip. It had the appearance of a leukoplakia that was slightly elevated above the surrounding mucous surface.

With the patient under local anesthesia the entire lesion was excised for histologic examination. There was slight superficial hyperkeratosis. The mucosa showed a decided acanthosis with a pseudo epitheliomatous hyperplasia. There was no invasion even though there were small keratin pearls deep in the epithelium. Little inflammatory infiltration was seen. Extending from the epithelium to the deeper muscle and infiltrating into the striated muscle fibers were large pale staining cells with small nuclei and granular cytoplasm. These cells resemble xanthoma cells, but stains for fat were negative. In some places these cells appeared to be degenerated muscle fibers.

## DISCUSSION

DR DON R PRINTZ There are only about 75 or 80 cases reported in the literature. There have been several complete articles in the *American Journal of Cancer*. Dr Klemperer stated (Am J Cancer 20 324 [Feb] 1934) in his review that about 44 per cent of all the cases are of the tongue and the rest are of the esophagus, the mouth and some of the trachea. An interesting thing to note in this is that it looked like a leukoplakia. In looking at the biopsy specimen, one saw a hyperplasia which might be mistaken for a bit of malignant growth. Stains of these xanthoma cells, as was noted in the write-up, were negative for fat. They contained no fat, and in looking at the cells more closely, one found that they were coarse and granular and took neutral stains. The cytoplasm was faint staining. The muscle seemed to be degenerated striated muscle. The theory offered by Elrikosoff was that they were the result of injury. Of several other theories offered, one considered the lesions neoplastic. However, none of them have been malignant, except in 1 case that was one of sarcoma. It was reported in the literature as myoblastic. The treatment is simply excision and cautery.

DR J E FISHER What was the diagnosis before the excision was done?

DR DON R PRINTZ The clinical diagnosis was leukoplakia with a possible malignant change.

DR J R DRIVER The lesion was more yellowish, and it was sharply delimited and raised a little more than one would expect of an area of leukoplakia. He had no other leukoplakia in his mouth. It looked like a little area of leukoplakia with xanthomatous degeneration. It was only after the histologic examination that the diagnosis was made.

#### A Case for Diagnosis (Epidermolysis Bullosa?) Presented by DR WOODROW W MURPHY and DR BURT HELD

R W, a 17 month old white boy, was seen in September 1945, because of a recurrent bullous eruption of the hands and feet. The lesions first appeared at the age of 5 days and have recurred about every three months since. New lesions appear for two to three weeks, remain for four or five days and then disappear by absorption of the bulla fluid. The mother has been treating them by rupturing the bullae as they form and applying solution of gentian violet medicinal to the base. The lesions are apparently asymptomatic. The formation of the bullae is not related to trauma.

There is no family history of similar lesions.

On the palmar surface of the fingers and hands and on the lateral side of one toe of the right foot are multiple thick-walled bullae 5 to 10 mm in diameter, containing a clear fluid. These lesions arise from apparently normal skin, with no evidence of surrounding inflammatory reaction. There is no evidence of disease of the nails.

A roentgenogram of the chest was normal. The hemogram and urine were normal. The Kline diagnostic and exclusion reactions of the blood were negative.

Histologic examination showed a strip of hyperplastic epidermis and in one small area a little superficial corium. There was moderate hyperkeratosis. The corium showed an infiltration of lymphocytes and edema. There was splitting at the junction of the epidermis and corium. Elastic tissue stains showed no fibers in this area.

## DISCUSSION

DR H N COLE I do not think that it is epidermolysis bullosa. In epidermolysis that has lasted as long as this, one would expect to find some milia in the area where the child is accustomed to have these lesions, and I could not find any at all. I am sure that I do not know what it is. Perhaps it might be a type of pustular mycosis. I do not think that it is epidermolysis bullosa.

DR J R DRIVER The disease started when the child was 6 days old and has been present ever since

DR J E RAUSCHKOLB The history obtained from the mother on the child's admission was that the child had lesions that were typically bullae on the exposed parts, particularly the hands and the area of the ankles. When examined last week there were two or three soft bullae that did not have a red or inflamed border. No one else in the family as far as she knows—the grandparents or her family or the sister or brothers of this child—have had any lesions like this. These lesions have been present periodically almost since birth, therefore we thought that probably this was one of the recessive type of epidermolysis bullosa. Clinically at the time we saw it, it certainly was not a dermatophytosis with the vesiculated border, there were clearcut bullae, unfortunately not present today

### PHILADELPHIA DERMATOLOGICAL SOCIETY

J M Schildkraut, M D, *Chairman*

Reuben Friedman, M D, *Secretary*

Sept 21, 1945

#### Actinomycosis Presented by DR FRANK C KNOWLES

S C, a white man aged 38, presents depressed, pigmented and granulating lesions of the anterior region of his thighs. Pigmented scars of healed lesions are present on both legs. The patient was admitted to the hospital on Sept 15, 1943, with a draining sinus of the right side of the face and spasm of the right masseter muscle. This followed incision and drainage of an abscess of the right cheek after apical infection of an upper molar on the right side in June 1943. Metastatic abscesses then developed in the extensor muscles of the forearms, followed by abscesses in the right temporal region. On Nov 15, 1943, he was readmitted to the hospital with multiple abscesses of the extensor surfaces of the thighs, the left gluteal region and the right supraclavicular region. During this time a gluteal abscess and uveitis developed. He was discharged on March 1, 1944, and readmitted on March 7, 1944, complaining of pain along the lower intercostal nerves.

Roentgenographic studies of the chest revealed infiltration of the pulmonary fields. A bacterial smear showed *Actinomyces*, and a culture revealed *Actinomyces bovis*. Two white cell counts of his blood recently performed revealed 9,450 and 8,200 cells respectively. The sedimentation rate of the blood on April 27, 1944, was 35 mm, and in September 1945 it was 19 mm. The histologic report was "chronic inflammation."

On Nov 5, 1943, the areas were incised and drained. The patient was given injections of penicillin on Dec 3, 1943 (10,000 units every four hours).

#### DISCUSSION

DR DONALD M PILLSBURY Has there been improvement since administration of penicillin was started? I have not seen any patients with actinomycosis treated with penicillin, but my impression is that those who responded had received larger doses. I think also that this patient may demonstrate possibly, if he has an abscess of any sort, that the use of penicillin alone, without surgical drainage of the abscess, may not be entirely effective. The diagnosis in this case is clinched.

DR JOHN F WILSON In spite of many tissue sections over a period of three years, not a single specimen showed actinomycosis. Cultures finally revealed the organism.

DR ISADORE ZUGERMAN I should like to suggest the use of streptomycin.

**Annular, Macular Syphilid** Presented by DR FRED D WEIDMAN and DR SIMON KATZ

T G, a Negro woman aged 40 years, presents on her chest irregular circular and oval rings with clear centers and also segments of circles which by coalescence form gyrate figures. The lesions have crinkly borders, are slightly scaly and show no infiltration. One week following her discharge from the hospital a month ago, following an operation for gallstones, the patient noticed a number of dark areas on both sides of her chest. A week later oval lesions appeared in the same regions.

The Wassermann reaction of her blood on Sept 10, 1945, was strongly positive. On Sept 14 and 18, 1945, she received an intravenous injection of 0.3 Gm and 0.45 Gm of neoarsphenamine respectively.

**DISCUSSION**

DR J V KLAUDER: I do not agree with the diagnosis. I think that it is parapsoriasis. My concept of the annular macular syphilid is that it is never a scaly lesion and never a diffuse lesion such as this. It must be an extremely rare disease, I have seen only 1 case in many years of observation. I should like to know on what basis the diagnosis was made. My concept is that it is always a rather localized, not diffuse lesion.

DR FRED D WEIDMAN: Dr Katz and I knew that we would have repercussions on this. Frankly, we did not feel that it was a case of so-called neurosyphilid, but we thought that that was the best way of securing a discussion of it—to throw out the challenge. This is not a diffuse eruption. The lesions are annular. Our first thought was that it might be a form of erythema multiforme, such as erythema perstans or the erythema chronicum migrans of Lipschutz, but the drawback to that was that there are definite atrophic pittings in the margins of these lesions, which seem to indicate a heavy degree of infiltration. Furthermore, against the idea of neurosyphilid is the fact that this eruption is bilateral and symmetric. So we were torn between these considerations. I have seen only 1 case of Unna's neurosyphilid, I think that Dr Klauder saw it, too, at a meeting of the American Dermatological Association in Washington, D C. It was presented as a case of leprosy, and then some one advanced the diagnosis of neurosyphilid of Unna. The eruption consisted of a solitary lesion on the chest. In that case there was not the degree of infiltration in the periphery that has been present in the early stages of this lesion. Dr Katz and I should like suggestions as to what this may be.

DR VAUGHN C GARNER: I may be wrong, but it seemed to be my impression that the neurosyphilid of Unna involves changes in the nerve supply of the skin rather than a definite connection with syphilis of the central nervous system. Is it not true that this patient has had two treatments for syphilis? Has there been any clinical improvement since treatment was instituted?

DR SIMON KATZ: We have not noticed any change.

**Keloids** Presented by DR MEYER L NIEDELMAN

N W, a white woman aged 24 years, presents on the dorsum of the left wrist a round, margined, elevated, irregular, erythematous and hard keloid measuring 3.5 by 4.5 cm. It is raised about 1 cm above the surface. The lesion interferes with free mobility of the wrist. Behind the left ear there is a keloid extending along the line of incision from which a skin graft was taken some time ago. The patient had a small ganglion of the dorsum of the left wrist. It was removed by operation in March 1944. Shortly thereafter, a keloid about the size of a dime developed at the site, with impairment of motion of the wrist. In May 1944, the keloid was excised surgically and the area covered with a graft from the left retroauricular region. Shortly thereafter, the present keloid developed on the wrist. It is accompanied with much itching and pain. A keloid formed at the donor site in the retroauricular area.

The patient received one roentgen ray treatment, 225 r with 3 mm aluminum filter, a week ago.

## DISCUSSION

DR A. STRAUSS I believe that Dr. Pfahler advises surgical excision of keloids and the use immediately after the operation of 400 r with a 1 mm. aluminum filter, to be followed within a week with 300 r and repeated in another week

DR MEYER L NIEDELMAN I believe that the surgeon erred originally in not following the graft up immediately with roentgenotherapy I believe now that roentgenotherapy is the method of choice

DR A STRAUSS Dr Pfahler has stated the belief that if plastic surgical treatment is to be done it should be done afterward

DR J M SCHINDKRAUT, Trenton, N J Sometimes keloids respond well to roentgenotherapy

DR THOMAS BULLERWORTH, Reading, Pa Has any one ever destroyed keloids of this size with solid carbon dioxide? I have removed small ones by this means

**Ulcers: Acute Pyogenic (?) Factitial (?) Anaerobic (?).** Presented by  
DR. FRANK C KNOWLES

O D, a white woman aged 23, presents on the right forearm a granulating ulcer about 1 cm in diameter, extending into the subcutaneous tissue A similar but larger ulcer is present on each gluteal region The lesion on the right forearm appeared several weeks ago, while the patient was receiving treatment with penicillin

About three months ago headaches, fatigue and malaise developed On Aug 17, 1945, her temperature was 101 F She was admitted to the hospital five days later There a sore throat developed She has lost 20 pounds (9 Kg) in the last year She had phlebitis of the left leg during the last month Her temperature, which has ranged from 99 to 104 F, has been normal since September 9

A blood cell count revealed a 67.3 per cent hemoglobin content, 3,700,000 erythrocytes and 13,350 leukocytes Bacterial culture of the vesicles showed *Staphylococcus aureus* and *Staphylococcus albus* The patient's serum agglutinated *Eberthella typhosa* in dilutions of 1 to 20 and 1 to 640

The patient received 150,000 units of penicillin

## DISCUSSION

DR DONALD M PILLSBURY The ulcer on the forearm is entirely compatible with diphtheria cutis, an entity with which I was unfamiliar before seeing it in the Army There was a great deal of diphtheria in the South Pacific area, particularly in Saipan, much more than in the European Theater of Operations The lesions are frequently sharply punched out, like this one, may be deep and may or may not have sequelae Sometimes the sequelae are severe I recall seeing 1 patient with a penile diphtheritic ulcer, in a hospital in England, who died of myocardial disease It may or may not be possible to demonstrate the organism The results of the Schick test are variable I think that it should be attempted here These patients will, of course, improve decidedly with penicillin therapy, local or otherwise Livingood and others have expressed the opinion that repeated formation of a bulla on a healed scar is highly characteristic of diphtheria cutis

DR J V KLAUDER Are the diagnoses positive in cases in which the organism is not demonstrated?

DR DONALD M PILLSBURY It has been necessary to make a presumptive diagnosis in many cases There have been many instances of myocardial sequelae and peripheral neuritis in such cases There is a particular tendency toward diphtheria of the skin in the hot climates It developed frequently in German prisoners, possibly because diphtheria toxoid immunization is rarely used in Germany and the general resistance of the German population to diphtheria is low These cutaneous lesions do not respond particularly well to diphtheria antitoxin It is given primarily to prevent sequelae, but treatment with salt solution and with penicillin are the methods of choice The scar of cutaneous diphtheria is one of the most sharply punched-out scars that one sees—more so than syphilis

**Malignant Melanoma** Presented by DR FRANK C KNOWLES

A A, a white woman aged 59 years, presents on the posterior portion of the right arm, in the right axilla, in the right upper scapular region and on the abdomen various-sized, firm, slightly tender subcutaneous tumors. One on the left side of the abdomen is grayish black. The patient, a cachectic woman, noticed pain in the left lower quadrant about five weeks ago. She then found a lump in the skin in this area which was hard and tender. There is a similar lesion on the posterior part of the right arm. Three weeks ago a dark lesion (black?) appeared under the right axilla and later on the right upper scapular region. This was followed by pain in the right breast, radiating to the back and down the right arm, it gradually became worse.

A blood cell count revealed a 55.4 per cent hemoglobin content, 2,700,000 erythrocytes, 5,100 leukocytes, 308,000 platelets, 75 per cent segmented polymorphonuclear leukocytes, 16 per cent medium and small lymphocytes, 6 per cent monocytes and 3 per cent disintegrated cells.

Dr G P Muller surgically removed a well encapsulated mass, about 4 cm in length and 3 cm in diameter, from the right axilla, lying deep in the tissue along the axillary artery and vein. The mass was opened and found to be filled with a blue-black colloidal material.

The histologic diagnosis on the biopsy specimen was malignant melanoma.

**DISCUSSION**

DR BERNARD L KAHN: How would one make the diagnosis clinically, without a biopsy?

DR J M SCHILDKRAUT, Trenton, N J: I do not know that one could make the diagnosis clinically. It might be suspected if the patient was losing weight and becoming cachectic. Perhaps the color of the lesion might arouse suspicion.

**A Case for Diagnosis** Presented by DR DONALD M PILLSBURY and DR E R CONSTANT

A white woman aged 44 years gives a history of the development of inflammatory papules and nodules all her life, usually on the neck, which would last from several months to a year. Some disappeared spontaneously, and others would have to be incised by herself or her husband and after draining would heal with scar formation. At the time the patient was first seen, July 9, 1945, she presented a nodule about 1 cm in diameter on the anterior aspect of her neck and also several smaller, nonfluctuating papules. Around the neck were a number of white, noncontractile scars with bizarre borders. Scars of previously removed lesions (1943) were noted over the right mandible (no report of biopsy available), on the posterior aspect of the right thigh (report of biopsy: lipoma) and on the left breast (report of biopsy: chronic cystic mastitis).

The nodule on the neck was excised, and the following histologic report was submitted by Dr Fred D Weidman:

"Speaking collectively, from the two halves of the lesion which appeared in the section, it was clear that an invaginated pocket of dense hyperkeratotic material occupied the summit of the lesion, incidentally, the keratotic material extended also into the orifices of some of the hair follicles.

"The entire epidermis was acanthotic and extremely irregular in the extent to which extensions pass from it into the corium. Indeed, some of them extended to the bottom of the section. Some of them appeared in the form of epithelial pearls.

"The stroma did not contain nearly so much lymphocytic infiltration as might be expected. The large numbers of dilated capillaries in the stroma were most unusual, so much so as to suggest that the lesion came from some highly vascular region like the lip. However, these vessels were not arranged in a fashion that is consistent with a hemangioma, but it is granted that they might represent a mild expression of vascular nevus. There was not the slightest evidence of formation

of a granuloma or other process that would seem to demand tests for bacteria. This lesion was an extremely slowly proliferative precancerous dermatosis that had passed over into malignant change of low grade. One cannot escape the diagnosis of a malignant growth with the pearly bodies lying at such a deep position, to say nothing of the active type of cell that is concerned in the other squamous cell infiltrations. This is the kind of cancer that I should expect to develop as the result of exposure to carcinogenic agents such as tar and which are known to regress spontaneously.

"The pathologic diagnosis was precancerous dermatosis with malignant change."

The following examinations and tests were performed and found to give results within normal limits: blood cell counts, urinalysis, basal metabolic rate, blood sedimentation rate and roentgenographic studies of the chest, abdomen and gastrointestinal and urinary tracts.

Smears and cultures of material from the removed gland were negative for tuberculosis or fungi. Bacteriologic studies were made both aerobically and anaerobically, and hemolytic *Staph aureus* was found in moderate numbers, a few short chain indifferent streptococci were found and a large colony of *Streptococcus fecalis* type was present.

The patient reacted moderately to 0.1 cc of staphylococcus ambotoxoid diluted 1:10 with isotonic solution of sodium chloride. She has received no active treatment.

#### DISCUSSION

DR J. V. KLAUDER: I suggest acne urticata as a possible diagnosis.

DR FRED D. WEIDMAN: I wish that I could reconcile the clinical picture with the one that I saw in the section. I made a report of precancerous dermatosis from what I saw. There must have been an additional lesion much larger than any appearing tonight, and that was sent to me for study.

DR DONALD M. PILLSBURY: You were seeing a late development of the process.

DR FRED D. WEIDMAN: I reviewed the section this afternoon. Ordinarily I should call the process a pseudoepitheliomatous hyperplasia, but I could not see the suppuration which is almost invariably present in that condition, and that is why I did not mention it in the original pathologic report. Joining up what I have seen tonight with the sections, I should say that probably the sections have no diagnostic significance but exhibit simply an active attempt at regeneration of the skin.

DR HERBERT J. SMITH: I agree with what Dr. Klauder said. I think that we all see these small, multiple, scarlike lesions which do not seem to amount to anything at all. We often find that such patients do have what the patient describes as a recurrent summer eruption, that is, *lichen urticatus*.

DR J. V. KLAUDER: I should suggest that this woman be given calcium therapy. I have thought that patients were benefited by such therapy. There is also a factitious element about this picture. The original lesions which she had were aggravated by picking after they appeared, which added to the scar formation. *Lichen urticatus* is too briefly described in modern textbooks for one to get an intelligent concept of it. It is best described in some of the older European textbooks, and the best description is the original one by M. Kaposi (*Ueber einige ungewöhnliche Formen von Acne [Folliculitis]*, *Arch f Dermat u Syph* 26:87, 1894). A discussion of this disease is also afforded by J. V. Klauder and F. D. Weidman (*Acne Urticata Polycythaemica, Positive Oxidase Reactions in Lesions Macroscopically and Microscopically*, *ARCH DERMAT & SYPH* 39:646-666, 1939).

DR JOHN F. WILSON: I first saw this girl a year and a half ago. She then had two or three superficial excoriations of the skin. There was nothing typical about the eruption. It seemed to me that she made more of it than was really there. Looking back, it certainly does seem to fit in with acne urticata. There is a definite element of neurotic excoriation to it. She certainly traumatizes the lesions, she frankly admits it.

**A Case for Diagnosis (Lupus Vulgaris?)** Presented by DR SIGMUND S GREENBAUM

M Y, a white woman aged 24 years, an average normal woman, intelligent and cooperative, presents on the right cheek a more or less circumscribed erythema with slightly visible and definitely palpable nodules, some of which are dark brown under glass pressure. There are no subjective symptoms. On the left side of the chin there is a scaly, well defined, pink, nickel-sized, nonpruritic area. The eruption is of two years' duration. It began as a small red papule on the right cheek. No treatment was given. It gradually spread to its present size. A similar lesion appeared on the left side of the chin two months after the original lesion. This was treated with ultraviolet irradiation a few months ago by a dermatologist. There is no pruritus.

The patient's mother is living and well at the age of 49 years, as is her father, at the age of 53 years. She has two brothers, aged 27 and 22 years, and a sister 15 years, all living and well. There is no history of the eczema-hay fever-asthma complex in the family. The patient has had the usual childhood diseases, including parotitis, and a tonsillectomy in 1938. She had a premature delivery, at seven months, of a stillborn child in 1944. She has gained 5 pounds (2.3 Kg) in the past two years.

A reaction to the patch test for tuberculosis and the serologic reaction of the blood for syphilis were negative. A complete blood cell count and a urinalysis gave normal findings.

**DISCUSSION**

DR BERNARD L KAHN I make a diagnosis of rosacea.

DR MEYER L NIEDELMAN I think that it is the Lewandowsky rosacea-like tuberculid. No pustules are present, the lesions are not centrally located, and no seborrhea is present. I should suggest an intradermal tuberculin test, which would aid in establishing the diagnosis.

DR ISADORE ZUGERMAN I found some follicular plugging present. I suggest the diagnosis of subacute lupus erythematosus.

DR VAUGHN C GARNER I favor the possibility of a rosaceaform tuberculid, from a clinical standpoint.

DR DONALD M PILLSBURY I think that it is of interest that the lesion on the left side of the chin was apparently similar to that on the right cheek. It would be well to have a biopsy. I should consider treatment with solid carbon dioxide.

DR FRED D WEIDMAN There is a deep-seated nodule at one place. If that occurred by itself, all of us would think of some condition of the sebaceous glands, perhaps a sebaceous cyst. I do not think that this is Lewandowsky's tuberculid, those are generally diffuse, while this is well confined to one area.

DR J V KLAUDER It impressed me as Lewandowsky's tuberculid. I do not know that the statement that it is too localized would exclude the diagnosis.

**Hemangioma** Presented by DR ARTHUR G PRATT, Camden, N J

V S, a white boy aged 6 years, on examination on May 16, 1939, presented a massive, elevated, ruby red hemangioma encircling the left forearm and covering the back of the left hand.

A roentgenogram on Dec 16, 1943, showed no disease of the bones of either forearm or hand.

Radium, to a total of 50 mg hours, was administered from June 7, 1939, to Oct 26, 1940. A total of twelve injections of quinine and urea hydrochloride was given from Dec 21, 1939, to Jan 30, 1941. There has been a good cosmetic result.

**DISCUSSION**

DR ARTHUR G PRATT, Camden, N J The reason for presenting this case was to try to get some discussion concerning the therapy of strawberry marks.

Some are thought to disappear spontaneously, without any treatment or with little treatment

DR MEYER L NIEDELMAN Anderson, in a recent article, claimed that 90 or 95 per cent of angiomas will disappear spontaneously before the sixth year. As to injection therapy, at the last meeting of the American Academy of Dermatology and Syphilology a death was reported in an infant due to cerebral thrombosis following injection with sodium morrhuate. I prefer the use of radium or solid carbon dioxide

DR THOMAS BULLERWORTH, Reading, Pa Large lesions may be treated by roentgen ray therapy I think that it is well to turn some of these cases over to men using heavily filtered roentgen ray, approaching radium in effect

DR MORRIS MARKOWITZ I think that only about 10 or 15 per cent disappear spontaneously

DR HERBERT J SMITH I should like to suggest that repeated treatment clears up these lesions If the needle is simply thrust into the lesion repeatedly, it will clear up

DR THOMAS BULLERWORTH, Reading, Pa Too often, I should say, treatment of these lesions with solid carbon dioxide gets one into trouble

**Iodide Dermatitis** Presented by DR FRED D WEIDMAN and DR SIMON KATZ

E T, a well nourished white woman aged 23 years, presents a fungating circular lesion, of four weeks' duration, on the middle of the chin, associated with submental adenopathy There is a punched-out ulcer on the right thigh There is a pea-sized papule in each temporal region There are three nodule-like lesions on the labia For the past three days the patient has been hoarse For one month prior to the onset of the eruption, she took a small quantity of a solution of potassium iodide (exact dose unknown) once daily The patient had previously received a course of treatment with oxophenarsine hydrochloride from Jan 8 1942, to Jan 22, 1942 The serologic reaction of her blood was reported negative at various times from April 13, 1942, to June 29, 1942 On Sept 12, 1945, it was reported positive (4 plus). Dark field examination of the serum from the lesion on the chin gave negative results A complete blood cell count revealed a 63 per cent hemoglobin content, 3,700,000 erythrocytes, 6200 leucocytes, 42 per cent neutrophils, 54 per cent lymphocytes and 4 per cent eosinophils

There is a history of having received "injections in the hip" for a period of six months ending in March 1945 She has taken sodium chloride internally

#### DISCUSSION

DR FRED D WEIDMAN An interesting feature of this case is the occurrence of the nodules on the vulva I should like to be informed about the frequency with which iodide lesions have been seen on the vulva

DR HERBERT J SMITH I never heard of an iodide eruption appearing on the vulva I think that the lesions are syphilitic

DR SIMON KATZ. This patient has received thirty-seven injections of oxophenarsine hydrochloride and thirteen injections of a bismuth preparation After she came home from the hospital, her mother thought that the best way to get rid of the infection was to give her iodide of potassium, and she gave her a glassful (of indeterminate dosage) every day Since she has taken the iodide, the hoarseness, the eruption on the mucous membranes, the lesion on her chin and the submental adenopathy have developed

DR HERMAN BELYMAN I think that it is iododerma I have never seen iodide lesions on the vulva, but Dr Greenbaum has reported oral lesions resulting from use of iodide. I do not see why this patient's clinical picture is inconsistent with a diagnosis of iododerma

## Book Reviews

**Pathology of Tropical Diseases** By Col J E Ash, M C, A U S, Director, Army Institute of Pathology, Army Medical Museum, and Sophie Spitz, M D, C S, A U S, pathologist, Army Institute of Pathology, Army Medical Museum Price, \$8 Pp 350, with 941 illustrations, 15 in color, on 257 plates Philadelphia and London W B Saunders Company, 1945

Although this splendid manual was composed primarily for students of tropical medicine and naturally was written from the point of view of the pathologist, a surprisingly large part of it concerns dermatology Since it is an atlas, an estimated 90 per cent of the pages consists of illustrations The text, although naturally and necessarily abbreviated, is none the less thoroughly brought down to date, it is gratifying to observe the manner in which essential material can be condensed

The senior author, Colonel Ash, has been active for a number of years in the educational program of the American Academy of Dermatology and Syphilology, and perhaps this association with dermatologists is partly responsible for the rich representation of dermatologic illustrations One might indeed suspect that special effort had been made to assemble as many dermatologic illustrations as possible There are few that are not original, and many are not paralleled elsewhere in print Incidentally, this atlas is one more tangible expression of the manifold activities which have raised the Army Institute of Pathology to such an enviable place in American medicine

The service to dermatology is directed where it is much needed, i e, toward the etiologic agent and the histopathology, which have been given much emphasis For example, there are scores of illustrations of aid in these respects in the text relating to smallpox, granuloma inguinale, lymphogranuloma venereum, verruga peruana, yaws, bejel, pinta and leprosy Naturally, the dermatologist is also informed as to the osseous and visceral lesions in the premises

Fungous diseases are exhaustively illustrated, in respect to not only the deep mycoses, as might be expected, but also the superficial ones The beautiful histologic sections of bullous dermatophytid and of the fungus in sections of onychomycosis, tinea versicolor, tinea capitis, favus and moniliasis illustrate this point The rich material concerning the deep mycoses again includes large numbers of illustrations of the cutaneous involvements All the foregoing compliments apply to the subjects of leishmaniasis, ground itch, creeping eruption, onchocerciasis, pellagra, scabies, chigoe, tropical ulcer and anhum, although in a more limited way

It is to be regretted that the authors did not follow the "Standard Nomenclature of Disease" in speaking of lymphogranuloma venereum They used the term "lymphopathia venereum"—which, incidentally, has incorrect Latin terminations

The publishers have done splendidly their share of the work The book is sturdily bound and is printed on enamel paper throughout The reproduction is superlative In short, all concerned have rendered a large service to dermatology, whether knowingly or not, by supplying so many and such splendid illustrations These can well serve as examples of the quality and the composition which should be aimed at when authors are planning to submit illustrations for publication to medical journals

**Cosmetics and Dermatitis** By Louis Schwartz, M D, and Samuel M Peck, M D Price \$4 Pp 189, with 20 illustrations New York Paul B Hoeber, Inc, 1946

In this publication the authors have attempted to systematize the knowledge of cosmetics and their effects They utilize the existing literature on the subject and their own wide personal experience to accomplish their purpose

The early sections of the book are devoted to the anatomy and physiology of the skin and percutaneous absorption of materials locally applied. The subject of dermatitis from cosmetics, including a discussion of occupational dermatitis among hairdressers and beauticians, is covered. In this section also is a useful partial list of chemicals and initial materials and cosmetics in which they may occur which may cause dermatitis.

Most instructive, perhaps, is the large section of the book devoted to the many different types of applications intended for use on the skin, sample formulas of these substances and their action.

A readily accessible bibliography follows each chapter.

The book contains much information on an important subject and should be valuable to the dermatologist.

**Treatment by Ion Transfer (Iontophoresis).** By D. Abramowitsch, M.D., and B. Neoussikine, M.D. Price, \$4.50. Pp. 200. New York: Grune & Stratton, Inc., 1946.

In the preface the authors state that the field of ion transfer has not received the careful and widespread application and evaluation which its preliminary results appear to warrant. They hope that the presentation of existing knowledge in this field will serve as a basis for further study and utilization of its possibilities.

This book has fourteen chapters, a fairly extensive bibliography and an index. The first part of the book, consisting of four chapters, discusses the historical development of ion transfer, the physical characteristics of the electric current, the effect of electrolytically introduced drugs and the methods of treatment. The second part of the book is divided into the use of iontophoresis in diseases of the nervous system, arthritis, lumbago and torticollis, scars and dermatologic conditions, diseases of the genitalia, diseases of the ear, nose and throat, ophthalmology, dentistry and miscellaneous conditions such as neoplasms, phlebitis and varicose ulcers.

In discussing iontophoresis in dermatologic conditions, which is the main interest of the reviewer, the authors cite on five pages reports from the literature on the results of iontophoresis. Thus, bromine ion transfer is reported beneficial in the treatment of pruritus of the perineum and the anus, a 10 per cent potassium iodide solution in poorly healing wounds and ulcers and a 10 per cent solution of zinc sulfate or copper sulfate in streptococcal and fungous infections of the skin. Iontophoresis is reported to be successful in the treatment of superficial scars by means of zinc and chloride or iodine.

The reviewer believes that the mere citing of beneficial reports from the literature will not convince the dermatologist of the value of iontophoresis. The only way to awaken enthusiasm in this modality is to report in detail the effect of iontophoresis in numerous cases and to compare the results with those obtained from treatment with simpler methods.

**Diseases of the Skin For Practitioners and Students.** By George Clinton Andrews, M.D., Associate Clinical Professor of Dermatology, Columbia University College of Physicians and Surgeons. Third edition. Price \$10. Pp. 937, with 971 illustrations. Philadelphia: W. B. Saunders Company, 1946.

The third edition of this excellent book has been thoroughly revised from beginning to end. It contains thirty-five chapters, each with an adequate bibliography at the end. As the author states, every page has been rewritten and more than sixty new diseases of the skin have been added.

One of the most useful features of any dermatologic textbook consists in the number and quality of illustrations. In this respect the book has a wealth of well chosen clinical and histologic photographs. With a few exceptions, they are excellent.

The author has taken unusual pains to follow the "Standard Nomenclature of Disease and Standard Nomenclature of Operations" This is a help to all students of dermatology

The reviewer was pleased to note that the so-called mixed type of leprosy was not discussed, as many physicians now have expressed the opinion that this does not exist

One of the new features of the book is a chapter by Mr Braestrup on roentgen ray physics applied in dermatology

The use of fairly heavy glazed paper throughout the book makes it possible to have good reproductions of illustrations The book is well written and up-to-date and is highly recommended for dermatologists as well as students and general practitioners

**Venereal Diseases in General Practice** By Svend Lomholt, M D Price 25 s  
Pp 231, with 78 black and white and 39 colored illustrations London H K. Lewis & Co, Ltd, 1946

The book is a revised English edition of a Danish textbook on venereal diseases This edition was completed immediately before the war and had just been printed when the German occupation of Denmark in 1940 broke off all communication between England and Denmark The advances made in the treatment of venereal diseases, particularly the use of intensive methods of arsenical administration in syphilis, the use of fever therapy in gonorrhea and the use of penicillin in the treatment of both gonorrhea and syphilis, are outlined in a supplement to the general text

In the discussion of syphilitic aortitis, exception may be taken to the simple statement that both arsphenamine and the metals are tolerated well, since this may be misleading, it is fairly generally accepted that more emphasis should be placed on initial treatment with metals and iodides prior to institution of arsenical therapy in the treatment of aortitis The subject of false positive serologic reactions, discussed in the chapter dealing with the Wassermann test, is dealt with but briefly, since the ever-growing list of diseases and conditions in which positive serologic reactions of the blood occur is not mentioned, of the tropical diseases causing positive serologic reactions, pinta should also be included

Dr Lomholt has covered the field of venereal diseases in a clear and concise manner and admirably accomplishes his purpose to give a readily accessible presentation of the subject to the general practitioner The publication should be well received by the specialist in this field The illustrations are uniformly excellent

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## CLINICAL USE OF A NEW ANTIHISTAMINIC COMPOUND (PYRIBENZAMINE) IN CERTAIN CUTANEOUS DISORDERS

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JAMES W JORDON, M D  
AND

NORBERT G RAUSCH, M D  
BUFFALO

IN 1927 Lewis<sup>1</sup> postulated that allergic reactions depend on or are produced by the liberation of a histamine-like substance (H substance) at the site of the reaction. Most investigators are of the opinion that histamine and the H substance are identical or nearly so. Many investigators have sought ways and means of neutralizing this H substance and thus preventing the sequence of events that occurs in allergic reactions. In 1932 Hill and Martin<sup>2</sup> reviewed the literature on antihistaminic substances and methods of preventing anaphylactic shock that had been described up to that time. None of these methods were effective. Since then, however, rapid progress has been made along this line.

Fourneau and Bovet, in 1933,<sup>3</sup> pointed out that the drug thymoxyethyl-diethylamine (929 F) had the ability to counteract the effects of histamine both in vitro and in vivo. Subsequently, this phenolic ether and others were studied for their antihistaminic effects by Bovet and Staub and their co-workers.<sup>4</sup> This chemical and one other were found

Read at the Sixty-Sixth Annual Meeting of the American Dermatological Association, Hot Springs, Va., June 10, 1946.

The pyribenzamine used in this study was furnished through the courtesy of Ciba Pharmaceutical Products, Inc., of Summit, N. J.

1 Lewis, T. *The Blood Vessels of the Human Skin and Their Responses*, London, Shaw & Sons, Ltd., 1927.

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3 Fourneau, E., and Bovet, D. Recherches sur l'action sympathicolytique d'un nouveau dérivé du dioxane, *Arch. internat. de pharmacodyn. et de thérap.* **46** 178-191 (Oct. 15) 1933, abstracted, *Compt. rend. Soc. de biol.* **113** 388-390, 1933.

4 Bovet, D., and Staub, A. M. Action protectrice des éthers phénoliques au cours de l'intoxication histaminique, *Compt. rend. Soc. de biol.* **124** 547-549, 1937. Staub, A. M., and Bovet, D. Action de la thymoxyethyl-diethylamine (929 F) et des éthers phénoliques sur le choc anaphylactique du cobaye, *ibid.* **125** 818-821, 1937. Ungar, G., Parrot, J. L., and Bovet, D. Inhibition des

(Footnote continued on next page)

to be the most effective of the group in the prevention of histaminic and anaphylactoid reactions in guinea pigs. The first of these, thymoxyethyl-diethylamine (929 F), was identical with that of Fourneau and Bovet. The second, N-phenyl-N-ethyl-N'-diethylethylenediamine, was called 1571 F and was found by Staub to be more effective than 929 F. These drugs, known as the Fourneau antihistaminic preparations, have been studied by a number of American authors, particularly Loew and his co-workers,<sup>5</sup> Wilcox and Seegal,<sup>6</sup> Rosenthal and Brown,<sup>7</sup> Rosenthal and Lambert,<sup>8</sup> and others<sup>9</sup> have confirmed the findings of Staub and her co-workers. The Fourneau antihistaminic drugs, although effective in preventing the sequence of events which histamine produces in tissue, were too toxic for human use. They led, however, to the development by Halpern,<sup>10</sup> in 1942, of a drug called "antergan," which chemically is dimethylaminoethylbenzylamine (2339 RP). This drug has been used clinically in European countries and has been reported on by Parrot,<sup>11</sup> DeCourt,<sup>12</sup> Celice and Durel,<sup>13</sup> Schnitzer,<sup>14</sup>

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6 Wilcox, H. B., and Seegal, B. C. Influence of an Ethylenediamine Derivative on Histamine Intoxication and Anaphylactic Shock in the Intact Guinea Pig and the Isolated Guinea Pig Heart, *J Immunol* **44** 219-229 (July) 1942.

7 Rosenthal, S. R., and Brown, M. L. Thymoxyethyl-diethylamine as an Antagonist of Histamine and of Anaphylactic Reactions, *J Immunol* **38** 259-266 (April) 1940.

8 Lambert, E. H., and Rosenthal, S. R. Liberation of a Histamine-like Substance on Stimulation of Sympathetic Nerves, *Proc Soc Exper Biol & Med* **44** 235-237 (May) 1940.

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12 DeCourt, P. Traitement de l'asthme par des bases antagonistes de l'histamine, *Presse med* **50** 773-774 (Dec 19) 1942.

13 Celice, J., and Durel, P. Eruptions seriques et antihistaminiques de synthèse, *Ann de dermat et syph (Bull Soc franç de dermat et syph)* **2** 370 (July-Aug) 1942.

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Gordonoff<sup>15</sup> and others. The drug was effective in urticaria, some types of asthma, serum sickness and other clinical manifestations of allergy. Certain side effects were noted such as restlessness, excitement, sleeplessness, accelerated heart beat, drug fever, apprehension, exanthemas and oliguria.

More recently Loew and his co-workers<sup>16</sup> in this country have studied a group of synthetic benzhydryl alkamine ethers. Two of these benzhydryl alkamine ethers were found to be far superior to the Fourneau antihistaminic compounds. They were nontoxic to guinea pigs and were capable of preventing the majority of animals from dying after exposure to atomized histamine. Oral administration was found to be effective. One of these drugs, beta-dimethylaminoethyl benzhydryl ether hydrochloride, was prepared for clinical use in human beings and has been marketed under the name benadryl. Among the American authors reporting clinical investigations on this drug are O'Leary and Farber,<sup>17</sup> Shaffer and co-workers,<sup>18</sup> Curtis and Owens,<sup>19</sup> Logan<sup>20</sup> and McElin and Horton.<sup>21</sup> O'Leary and Farber reported that 9 out of 15 patients with acute urticaria received almost complete relief and 5 others improved. There was one failure. In chronic urticaria, 25 out of 35 patients received almost complete relief, while 7 were improved and 3 were not benefited. Shaffer and associates reported that 7 out of 8 patients with urticaria were benefited. Curtis and Owens stated that 11 out of 18 patients with acute urticaria secured decided relief, 3 patients with chronic urticaria were improved and 4 received little or no benefit. Shaffer and colleagues stated that 1 patient with atopic dermatitis was relieved but that the drug had no effect on neurodermatitis or dyshidrotic eczema. Logan employed benadryl in treating allergic

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19 Curtis, A. C., and Owens, B. B. Beta Di Methylaminoethyl Benzhydryl Ether Hydrochloride (Benadryl) in Treatment of Urticaria, *Arch Dermat & Syph* **52** 239-242 (Oct) 1945.

20 Logan, G. B. The Use of Benadryl in Treating Some of the Allergic Diseases of Childhood, *Proc Staff Meet, Mayo Clin* **20** 436-438 (Nov 14) 1945.

21 McElin, T. W., and Horton, B. T. Clinical Observations on the Use of Benadryl. A New Antihistamine Substance, *Proc Staff Meet, Mayo Clin* **20** 417-429 (Nov 14) 1945.

diseases of childhood and reported that 9 out of 12 patients with seasonal hay fever had excellent or good results, while there was a questionable result in 1 and no effect in another. In his series, bronchial asthma was not affected, and in urticaria and vasomotor rhinitis the drug had a palliative effect. All these authors reported rather frequent mild to serious side effects from the administration of benadryl. O'Leary and Farber had 18 patients out of 50 in which symptoms from the drug developed, whereas McElin and Horton noted that in 54 patients out of a total of 74 who received benadryl orally, there developed side effects, and in one third of their patients receiving benadryl intravenously there developed symptoms from the drug. The commonest symptoms were sleeplessness, dizziness, dry mouth, nervousness, urinary frequency, epigastric distress, vomiting, weakness, vertigo, drowsiness and muscular pains. None of the authors reported any serious reactions to the drug.

A new group of compounds has recently been prepared by Mayer, Hutterer and Scholz.<sup>22</sup> These are known chemically as pyridylethylenediamines. One of these (N'-pyridyl-N'-benzyl-N-dimethylethylenediamine) was called pyribenzamine. These authors found that this drug neutralized the effects of histamine on an isolated strip of guinea pig intestine. It was found effective against histamine-induced asthma in guinea pigs and against anaphylactic shock produced by the injection of horse serum in guinea pigs. The antianaphylactic and antihistaminic activity and toxicity of this drug were studied by Rennick, Chess, Hays, Mathieson, Mayer and Yonkman.<sup>23</sup> The drug was found effective against intratracheal injections of histamine in guinea pigs. Wheals produced by the intracutaneous injection of histamine in rabbits could be prevented by the intravenous administration of the drug or by gastric instillation. The drug was relatively nontoxic for white mice, white rats and rabbits, and human beings tolerated the drug well. Hays and

22 Mayer, R. L., Hutterer, C. P., and Scholz, C. R. Antihistaminic and Antianaphylactic Activity of Some A-Pyridino-Ethylenediamines, *Science* **102** 93-94 (July 27) 1945, *Federation Proc.* **4** 129 (March) 1945.

23 Rennick, B., Chess, D., Hays, H. W., Mathieson, D., Mayer, R. H., and Yonkman, F. F. The Antianaphylactic and Antihistaminic Activity and Toxicity of N'-Pyridyl-N'-Benzyl-N-Diethyl-Ethylenediamine HCL, *Federation Proc.* **4** 133-134 (March) 1945. Yonkman, F. F., Chess, D., Mathieson, D., and Hansen, N. The Antihistaminic Action of N'-Pyridyl-N'-Benzyl-N-Dimethyl-Ethylenediamine HCL (63c) in Relation to Salivation, Retraction of the Nictitating Membrane, Mydriasis, Lachrymation and Blood Pressure in Cats, *ibid.* **4** 143 (March) 1945. Yonkman, F. F., Hays, H. W., and Rennick, B. The Protective Action of N'-Pyridyl-N'-Benzyl-N-Dimethyl-Ethylenediamine HCL (63C) Against Horse Serum Anaphylaxis in Dogs, *ibid.* **4** 144 (March) 1945. Mathieson, D., Hays, H. W., Chess, D., Cameron, A., and Yonkman, F. F. Acute and Chronic Toxicity Studies of Pyribenzamine HCL (N'-Pyridyl-N'-Benzyl-N-Dimethyl-Ethylenediamine HCL), *ibid.*, to be published.

Rennick found that the drug protected against horse serum anaphylaxis in dogs in 50 per cent of cases. The drug administered to white rats for a period of five months showed no deleterious effects on the erythrocytes, white cells, hematocrit values, body weight, appetite, reproductive capacities, gastrointestinal functions or general appearance.

Mayer<sup>24</sup> has reviewed the literature on substances with specific antihistaminic activity, and he has compared the activity of these various related chemical compounds. Loew and his co-workers compared the action of benadryl with 1571 F. From an experimental laboratory standpoint, the action of pyribenzamine and benadryl has been compared with the action of 1571 F and 929 F by means of four principal laboratory experiments, as follows: (1) neutralization of the effect of histamine on guinea pig intestine, (2) neutralization of the effect of intravenously injected histamine, (3) prevention of anaphylactic shock and (4) determination of the effect on histamine-induced asthma. In regard to the first experiment, with guinea pig intestine, Loew<sup>25</sup> found that benadryl was fifteen to twenty times as effective as 1571 F. Mayer found that pyribenzamine was one to ten thousand times as effective as 929 F. Since it was well known that 1571 F was approximately 25 per cent more effective than 929 F, it is apparent from these analogous experiments that pyribenzamine is far more effective than benadryl. As regards the second experiment, with intravenously injected histamine, benadryl was found to be twice as effective as 1571 F, whereas pyribenzamine was twenty to twenty-five times as effective as 1571 F, and it might be added that antergan was found to be ten times as effective as 1571 F. Here again pyribenzamine demonstrated its superiority. Concerning the third experiment, on prevention of anaphylactic shock, it did not appear from the work of Loew and Kaiser<sup>25a</sup> that benadryl was much more effective than 1571 F, while Mayer demonstrated that pyribenzamine was two to three hundred times as effective as 1571 F. Finally, as regards the fourth experiment, on histamine-induced asthma, Loew and his co-workers<sup>5</sup> found benadryl twice as effective as 1571 F. Mayer demonstrated that pyribenzamine was several times more effective than 1571 F. In summary, according to comparative laboratory experiments which Mayer<sup>24</sup> and others have done with pyribenzamine and antergan and Loew and his co-workers with benadryl, pyribenzamine apparently stands superior, antergan second and benadryl third.

24 Mayer, R. L. Substances with Specific Antihistaminic Activity, *J. Allergy*, to be published.

25 (a) Loew, E. R., and Kaiser, M. E. Alleviation of Anaphylactic Shock in Guinea Pigs with Synthetic Benhydryl Alkamine Ethers, *Proc. Soc. Exper. Biol. & Med.* 58:235-237 (March) 1945. (b) Loew, Kaiser and Moore<sup>16a</sup>

Arbesman, Koepf and Miller<sup>26</sup> have reported recently that in studies on guinea pigs and human beings histamine wheals showed a definite decrease after the administration of 50 to 150 mg of pyribenzamine orally in 14 out of 22 patients. Four out of 6 allergic patients showed a definite decrease in the size of histamine-induced wheals. Twenty-four patients were tested with a series of allergens and retested forty-five minutes after receiving 100 mg of pyribenzamine orally. Fourteen of the 24 showed a definite decrease in the size of the wheals following the use of pyribenzamine. Reactions in passively sensitized areas of skin were also decreased by pyribenzamine. Koepf, Arbesman and Munafo,<sup>27</sup> in studies of toxicity in dogs, noticed no serious toxic effects. Arbesman, Koepf and Lenzner<sup>28</sup> have recently reported on a clinical study of 277 patients with various allergic disorders. The average adult dose varied from 100 to 400 mg daily, the average dose for children was half that amount. As much as 1,200 mg of pyribenzamine was given in twenty-four hours without any serious untoward effects. All medication was given orally. There was no effect on blood components, blood pressure or urine. Pyribenzamine prevented constitutional reactions from allergens to which the patients were sensitive, including urticarial reactions. Twenty-three of 24 patients with allergic rhinitis due to grass pollens were relieved of their symptoms, and 88 per cent of patients with ragweed hay fever were relieved. Seven of 16 patients with bronchial asthma associated with hay fever obtained relief from the asthma. Eighteen of 34 patients with perennial allergic rhinitis of extrinsic origin were relieved, 6 of 14 with perennial intrinsic rhinitis were relieved, 9 of 24 patients with extrinsic bronchial, seasonal asthma were relieved, and only 1 of 4 with intrinsic bronchial asthma was relieved. Fourteen out of 15 patients with acute urticaria were relieved, and 33 of 44 patients with chronic urticaria were benefited. They noted that several patients with atopic dermatitis obtained rather decided relief from pruritus when taking the drug. In 3 patients with urticaria due to hypersensitivity to cold, urticaria failed to develop on exposure to cold while they were taking the drug. In regard to drug reactions, in 66 per cent of their patients no symptoms developed, only 5.4 per cent discontinued the drug because of undesirable side effects. The commonest of these were sedation, drowsiness and fatigue. A few patients complained of dizziness, faintness and headache and, on rare occasions,

26 Arbesman, C. E., Koepf, G. F., and Miller, G. E. Some Antianaphylactic Properties of Pyribenzamine N'-Pyridyl-N'-Benzyl-Dimethyl-Ethylenediamine-Mono-Hydrochloride, *J. Allergy*, to be published.

27 Koepf, G. F., Arbesman, C. E., and Munafo, C. Chronic Toxicity of Pyribenzamine (N'-Pyridyl-N'-Benzyl-Dimethyl-Ethylenediamine-Mono-Hydrochloride), *J. Allergy*, to be published.

28 Arbesman, C. E., Koepf, G. F., and Lenzner, A. R. Clinical Studies with Pyribenzamine, *J. Allergy*, to be published.

nausea associated with emesis. A few complained of dryness of the mouth, and in 1 dermatitis medicamentosa developed.

#### CLINICAL STUDIES

In this paper, we wish to report the effects of pyribenzamine on patients presenting various cutaneous disorders and also the effect of the drug on wheals produced by the intradermal injection of allergens in patients with atopic dermatitis. A total of 122 patients was given the drug, and of these 89 were followed sufficiently long so that we could evaluate the effects of the drug.

*Acute Urticaria* There were 34 patients with acute urticaria. The follow-up was satisfactory in 24 of these. Pyribenzamine, in doses from 100 to 400 mg per day, was prescribed, and the drug was taken from two to fourteen days. Twenty-three of the 24 patients obtained prompt and definite relief of symptoms. It should be noted at this point that approximately the same percentage of patients obtained relief from benadryl. Nineteen of the 24 patients were improved 50 per cent within twenty-four hours and free of urticaria in less than ten days. Four patients were at least 50 per cent improved in four days and free of eruption in fourteen days. In 3 of the latter 4, the urticaria returned twenty-four hours after the drug was stopped but the urticaria was controlled by readministration. One patient with acute urticaria believed to be due to codeine in a cough syrup experienced no relief from the drug. This was our only failure in acute urticaria.

*Chronic Urticaria* Twenty-three patients with chronic urticaria were given pyribenzamine. The dose varied from 200 to 300 mg per day, and the period during which the drug was taken varied from six days to six months. Fifteen of these patients were followed adequately. Nine of the 15 were definitely benefited, whereas 6 patients reported no relief of symptoms. This result is essentially the same as that obtained with benadryl. In 6 of the 9 patients benefited by the drug, a recurrence of the urticaria developed within twenty-four hours after use of the drug was discontinued, but they again experienced relief when the drug was readministered. One patient had had urticaria for four months and took 200 mg of pyribenzamine daily for fourteen days, the symptoms completely disappeared within forty-eight hours and have not recurred.

*Atopic Dermatitis (Investigative Studies)* Sixteen patients with a chronic atopic dermatitis were studied in order to determine the effects of pyribenzamine on wheals resulting from the intradermal injection of a series of allergens. The allergens used were sheep wool, mixed feathers, milk, cat hair and three dilutions of egg white. The wheals resulting from these intradermal injections were observed and measured.

at the end of fifteen minutes. Patients were then given 100 mg of pyribenzamine and one hour later were retested with the same allergens as those which produced positive reactions in the original test. Of the 16 patients who received the intradermal injections, in 15 wheals developed to one or more of the allergens. In 7 of the 15, pyribenzamine produced no demonstrable diminution in the size of the wheal. Eight of the fifteen showed a decrease in the size of the wheal of 33.3 per cent or more. Two of the 8, following the ingestion of pyribenzamine, had no wheals on the second series of tests. On the basis of these experiments, we were unable to predict the outcome of the clinical use of pyribenzamine in these patients.

*Chronic Atopic Dermatitis (Effect of Pyribenzamine on Symptoms)*

Thirty-five patients with chronic atopic dermatitis were given pyribenzamine in doses of from 100 to 400 mg daily for periods which varied from two weeks to four months. In the case of children, the dose varied in proportion to the body weight. Thirty of these patients were followed sufficiently long to determine the effects of pyribenzamine on the course of their disease. Nineteen of the 30 received definite relief of pruritus to the extent of at least 50 per cent. Three of the 19 experienced relief of pruritus within twenty-four hours. The remaining 16 patients were decidedly improved within a two week interval. In 16 of the 19 patients, itching recurred when the drug was stopped and was again relieved when the drug was readministered. In 3 of the 19 patients, the dermatitis disappeared within six weeks and has not recurred to date. It must be stated that all these patients received the usual routine treatment with topical applications and advice regarding the avoidance of common water-soluble protein allergens. Some patients deliberately stopped taking the drug or their supply ran out, and these patients felt that there was a prompt flare-up of the itching. Four of the 7 patients who showed no change in allergen-induced wheals after receiving 100 mg of pyribenzamine were adequately followed. In 3 of these the pruritus was improved at least 50 per cent while taking the drug, and in 1 of these the eruption disappeared fifteen days after medication was started. There was, therefore, no correlation between the effects of pyribenzamine on allergen-induced wheals and clinical improvement. It was further noted that in the case of the 8 patients in whom pyribenzamine definitely diminished the size of allergen-induced wheals only 4 of these were benefited while taking the drug. This further demonstrated the lack of correlation between the effects of the drug on allergen-induced wheals and the results obtained clinically from the administration of the drug. It is our opinion that pyribenzamine is definitely palliative for approximately two thirds of the patients with chronic atopic dermatitis.

*Dermatitis Venenata* Fifteen patients with dermatitis venenata of long duration, most of whom were originally patients with industrial dermatitis, were given pyribenzamine in doses up to 400 mg per day. In none of these did the drug appear to influence in any way the course of the eruption, nor did it produce any relief of symptoms.

*Physical Allergy* Two of our best results were in patients who presented examples of severe physical allergy of long duration. The first patient was a woman 50 years of age who had had severe sunlight urticaria for eighteen years. She had received medical attention from outstanding internists and had received every form of therapy known to us and to many other consulting dermatologists. Laboratory studies of every conceivable type had given uniformly normal results. On a trip to Florida the past winter, minimal exposure to bright sunlight produced the usual papular urticarial lesions. On each day thereafter, 100 mg of pyribenzamine taken before and after exposing herself to sunlight for periods of from two to four hours completely prevented the development of urticarial lesions. Furthermore, the existing lesions, which usually healed in ten to fourteen days, disappeared within two to three days. Subsequent exposures to bright sunlight without pyribenzamine medication caused the usual urticarial lesions to appear. The second patient, a woman aged 53, had suffered from urticaria due to cold for thirty-three years. During this time, she had had countless episodes of giant urticaria involving all the exposed parts. Exposure to cold water, either in the tub or for purposes of swimming, had brought on collapse, with a loss of consciousness, on three occasions. Numerous allergy tests and attempts at desensitization had given unsuccessful results. She had been unable to eat ice cream for thirty-three years. She had had as many as twenty-two injections of epinephrine in a twenty-four hour period. Tests with small ice cubes produced erythema after fifteen seconds and severe urticaria after thirty seconds. Following the ingestion of 100 mg of pyribenzamine, tests with small ice cubes showed extremely slight erythema at thirty seconds and only slight urticaria after sixty seconds. This patient has had complete relief by taking 50 to 100 mg of pyribenzamine before exposing herself to cold in any form. For the first time in thirty-three years, she is able to eat a large dish of ice cream with impunity.

*Dermatitis Herpetiformis* Four patients with dermatitis herpetiformis disease have been followed sufficiently for us to draw conclusions regarding the effect of pyribenzamine on the course of their eruption. They received from 200 to 300 mg of the drug daily. Three of the 4 patients had almost complete relief of pruritus and burning while taking the drug, and the eruption healed. After observation, however, we were not able to state that the relief was any greater than that

experienced following the ingestion of sulfapyridine although it was much more prompt

*Miscellaneous Conditions*—One patient with rather extensive insect bites secured prompt relief from itching following the administration of pyribenzamine

#### REACTIONS TO PYRIBENZAMINE

In our experience reactions to pyribenzamine severe enough to be noted by the patient without suggestion were extremely rare. We purposely confined our questioning of the patients to one point, namely, whether they had noted unusual symptoms after the ingestion of the drug. Only 4 patients out of a total of 89 we were able to follow noted any disturbance. One patient complained of headache, another felt drowsy, 1 had nausea and the fourth had nausea and vomiting. The last patient was the only one that had to discontinue use of the drug although he had taken it steadily for a period of four months. Our figures regarding reactions are certainly at variance with those of Koepf, Aibesman and associates. Part of this may be explained by the fact that we did not use, in general, as large doses as they employed. It is our opinion, from our own results and in comparison of reported reactions from benadryl in the literature, that reactions from the use of pyribenzamine are considerably less than those after use of benadryl when given in comparable dosage in the same type of case.

#### COMMENT

It is evident that the introduction of new antihistaminic compounds which can be administered by mouth has opened a totally new field in the palliative therapy of many allergic and allied diseases. We may expect further antihistaminic drugs to be introduced, perhaps far exceeding the value of our present preparations. So far, there are three antihistaminic compounds of outstanding merit, namely, antergan, benadryl and pyribenzamine. It is as yet too early to state which of these three drugs will eventually be shown to be superior from all standpoints. From an experimental laboratory standpoint and our own clinical experience, pyribenzamine appears to be the drug of choice.

#### CONCLUSION

1. Rapid progress has been made in the past thirteen years in the development of antihistaminic compounds. The three most effective compounds developed to date are antergan, benadryl and pyribenzamine.

2. Clinical studies on dermatologic conditions by various investigators indicate approximately the same degree of clinical benefit from each of the drugs. Almost all patients with acute urticaria are relieved, about two thirds of those with chronic urticaria are benefited and somewhat

more than one half of the patients with chronic atopic dermatitis are improved. Three out of 4 of our patients with dermatitis herpetiformis obtained relief.

3 In 2 cases of severe physical allergy pyribenzamine produced prompt and complete relief.

4 There did not seem to be any correlation between the effect of pyribenzamine on allergen-induced wheals and the clinical course of the patient after receiving pyribenzamine.

5 In our opinion, reactions to pyribenzamine are minimal and seldom necessitate stoppage of the drug.

### ABSTRACT OF DISCUSSION

DR HAMILTON MONTGOMERY, Rochester, Minn. The experience of my colleagues and me in the Department of Dermatology of the Mayo Clinic concurs and supports in the main what Dr Osborne has said about pyribenzamine. Dr O'Leary and Dr Farber have recently reported their experience with patients with various types of cutaneous diseases treated with benadryl. Dr Brunsting has reported on a series of 215 patients with various dermatoses treated with pyribenzamine. It is our impression that pyribenzamine is slightly superior to benadryl, because, although dose for dose they act about the same, the side reactions from benadryl are more frequent and severer than those from pyribenzamine. Dr Brunsting's experience in cases of dermatitis venenata (contact dermatitis) differs from that of Dr Osborne in that there were a good many cases in which there was some relief from the pruritus, but no significant influence was noted on the dermatitis per se. Five patients with dermatitis herpetiformis received no benefit from pyribenzamine. In patients in the early phases of acrosclerosis (scleroderma and Raynaud's disease), with either benadryl or pyribenzamine Dr O'Leary obtained moderate temporary improvement in approximately 25 per cent of the cases, resulting in relaxation of the skin and restoration of some of the lost function of their fingers and hands. Both drugs are effective in relieving the symptoms of pruritus from urticaria in 85 to 90 per cent of the two series of cases. The response, however, is usually symptomatic and palliative and requires continued use of the drugs, however, an occasional patient is encountered who is apparently cured of chronic urticaria after using either drug for several weeks. The same effects are noted in angioneurotic edema. Pyribenzamine has a beneficial effect of producing slight drowsiness, which in itself is beneficial in obtaining relaxation in cases of urticaria. In the group with atopic eczema, a small percentage have derived relief from the severe paroxysms of pruritus. No doubt the soporific effect of the drugs also helps these patients through the recurring exacerbation.

DR FRED WISE, New York. When Dr Osborne speaks of dermatitis venenata, does he refer to plant poisoning or contact dermatitis, or does he include both?

DR GEORGE C ANDREWS, New York. In addition to the diseases that have been treated successfully by benadryl, I have been fortunate enough to have good results in the treatment of localized hyperhidrosis of the axilla and localized hyperhidrosis of the hands and also in erythema nodosum. In 2 cases the conditions cleared up in twenty-four hours, and as long as the patients took benadryl they were free from any symptoms or any nodules. I thought that it would be

interesting to add those two diseases to the list, particularly hyperhidrosis, which is such a difficult condition to cure

One of the patients with hyperhidrosis was an x-ray technician and had had a great deal of roentgen ray therapy. She had been treated with diets and all kinds of remedies, including bromides and other sedatives. Nothing did her any good, but use of benadryl relieved her immediately.

DR MARION B SULZBERGER, New York. What I have to say is confirmation of what the presenters have said, with perhaps a few minor additions.

As Dr Osborne said, this drug, pyribenzamine, was first introduced and studied by Dr R L Mayer, a former assistant of Professor Jadassohn, who is a well trained dermatologist as well as an excellent chemist.

Because of my friendship with Mayer, he submitted this drug to me early, and both at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital and in the private practices of its staff members, pyribenzamine has now been given a trial on several hundred patients. There are just slight variations between our findings and those of Dr Osborne and collaborators. In the few patients with dermatitis herpetiformis treated, we, like the physicians at the Mayo Clinic, were not particularly impressed with the benefits. It may be, however, that when a larger series has been treated these differences in results will be ironed out.

Again in adult atopic dermatitis we were not impressed, although an occasional patient did well. I had the impression that the earlier the case and the younger the disease, the better the results with pyribenzamine. But this drug is by no means the answer to the control of this disease or even the control of itching in this eruption. Only an exceptional patient with atopic dermatitis does really well, a few patients get moderate or questionable benefit, and many in our experience get no benefit whatsoever up to the limits of the tolerated doses.

I think that we are just at the beginning of a great development and will see significant advances in and wider application of drugs of this series. In my opinion, drugs of this type are going to be used in a large variety of chronic diseases, and in these diseases the patients will be taking these drugs more or less continuously, because these agents apparently allay the symptoms and reduce the manifestations without producing cures, as far as we can tell today. For this reason and because of the chemical and biologic attributes of these compounds, I think that it is necessary for patients taking these drugs to remain under constant and close medical control.

I think that if enough patients are treated with these drugs it is to be expected that in a few persons some more serious unoward effects (for example, of the type of blood dyscrasias) will be found sooner or later. It was the awareness of this possibility that limited the number of the patients included in our studies. We have not treated as many patients as we otherwise would, because we have made it a point to examine every patient once a week while taking the drug, including a complete blood cell count and differential count and examination of urine. I am convinced that, for the time being, all physicians should insist on this procedure. Otherwise, I am afraid that there may be unpleasant happenings for which we will be held responsible.

I should like to point out that there are many possible future uses of these drugs, as indicated by their trial in the sclerodermas and the acroscleroses, mentioned by Dr Montgomery. In this connection, lupus erythematosus must be mentioned, and, in particular, the conditions which are definitely made worse by exposure to light. It is certainly conceivable that in such cases the use of this

drug might be indicated. I have just started treating 1 such patient and have as yet no results to report. There are many other cutaneous and internal diseases in which these agents might contribute a logical form of treatment. I shall mention only dermatomyositis (1 of our patients did well), many forms of drug reactions and periarteritis nodosa.

Another use of the drug is in cutaneous testing. It is known that when one is testing the skin for wheal reactions one sometimes cannot read the results of the test because of the dermatographism. Each site tested produces a traumatic wheal. That traumatic wheal can be inhibited by adequate doses of pyribenzamine or benadryl, but the greater stimulus to whealing which is exercised by application of the allergen to which the patient is sensitive will usually break through the inhibitory action of those drugs. In this way, by a proper dose of one of these drugs, the false positive reactions due to traumatic whealing can be suppressed and the wheal reactions to the allergens will come through and can be recorded.

DR RICHARD S. WEISS, St. Louis. I should like to ask Dr. Osborne a question concerning the future supply of pyribenzamine. I tried to get a supply for experimental purposes but was informed that the company had only a limited amount for this purpose. I am glad to be informed that the drug is relatively nontoxic and hope that all of us will be able to use it shortly.

DR EARL D. OSBORNE, Buffalo. Time did not permit me to give some of the details, and I had to eliminate a great deal of the clinical work that has been done by Koepf and Arbesman. Dr. Sulzberger brought up the question of blood cell counts. Koepf and Arbesman have done all sorts of clinical and laboratory investigations in a large series of cases. Twelve hundred milligrams per day has been given without in any way affecting the laboratory tests. So far, at least, pyribenzamine has been shown to be of low toxicity to animals and human beings.

I think that it is important that we all read papers on this subject when they are published. Most of the work on this drug, by the way, is not yet published, except the work by Mayer and his associates. The other is in press now and will be out shortly.

One important thing about pyribenzamine and benadryl, too, is the way the drug is administered. Some men have the idea that all one has to do is to give 5 mg. every three or four hours. That may be all right in the chronic urticarias, but in treating atopic dermatitis we found it much better, since practically all the scratching and rubbing is at night, to give 100 mg. before retiring, and if the patient awakened during the night to give 100 mg. more and perhaps only 50 mg. two or three times during the day. Even that may not be necessary.

We were discouraged at first in atopic dermatitis. We felt that we were getting hardly any response, but after the passage of two or three weeks and the gradual reduction in the scratching index, as you might call it, those patients began to improve, and far more rapidly than would be naturally expected in the average case of atopic dermatitis. Our good results in atopic dermatitis vary from 50 per cent to 66.6 per cent.

Regarding the cases of dermatitis venenata, those were all cases of chronic industrial dermatitis.

In regard to hyperhidrosis, we had 1 patient who noticed prompt relief of hyperhidrosis, and Koepf and Arbesman have had a similar one.

## DERMATOLOGIC PROBLEMS IN A STAGING AREA STATION HOSPITAL

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AND

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**T**HE problems associated with the handling of diseases of the skin in a staging area station hospital are not of the type to which the average physician or dermatologist had previously become accustomed. To complicate further the care of the soldier in such a hospital, medical care and hospitalization had to be geared to the function of the camp. In this, the processing and subsequent departure of troops influenced treatment to a great degree. On arrival at the staging area from any part of the country, the soldier had just completed a train trip of perhaps one hundred and eight hours and was immediately processed preparatory to his departure. This frequently meant that any eruption not disabling or apparent was not treated by the soldier for almost a week. Then, when he was free from his numerous routine duties, the attention of the medical officer was called to a disease aggravated by neglect.

The dermatologic section at this station hospital was a part of the medical service and was under the supervision of a single medical officer, who was the chief of the section. The staff, although variable, was composed of two nurses, a trained civilian technician and at least two specially trained enlisted ward attendants.

Although the venereal section was a subdivision of the medical service, syphilitic patients were handled at this station hospital by the urologists, and therefore a report on them will not be included in this paper. In accordance with army procedure, all patients reported first on sick call each morning at their respective dispensaries, where the medical officer decided which ones were to be referred to the clinics and which admitted to the hospital. This weeded out many of those with minor dermatoses. The procedure has been that except in unquestionable cases no patient with a disease of the skin was admitted directly to the hospital without first being seen by the dermatologist. This eliminated many unnecessary hospitalizations.

From its inception, in June 1942, until Sept 1, 1945, this staging area station hospital admitted 52,788 patients, of whom 38,209 were admitted to the medical service. Of these, 2,968 had diseases of the skin. Thus 5.6 per cent of all the hospitalized patients and 7.7 per cent of all the patients hospitalized by the medical service were admitted to the dermatologic section. In addition to those of the inpatients service, 7,183 patients were seen during this period in the dermatologic outpatient clinic.

This series does not present a cross section of persons with dermatoses in the percentages usually expected in civilian practice. This is due partly to earlier elimination of persons with certain diseases of the skin by induction boards and in part to weeding-out of those with minor ailments by the dispensary surgeons. uncomplicated nondisabling diseases treated without a dermatologic consultation. The number of patients visiting the clinic was kept at a minimum by return visits being scheduled at intervals of at least seven to ten days unless the disease was of such a nature that a decided spread or exacerbation was to be anticipated. In this way, most of the patients seen were making their first visits. This enabled the dermatologist to devote more time to each patient, resulting in the eliciting of fuller histories and the making of thorough physical examinations.

In the staging area, as was mentioned earlier, problems were present, the chief of which was the early departure of the soldier for overseas duty. As in most army installations, the soldier either was or was not fit for duty. He was never placed "in quarters." The soldier seen for the first time after a week in camp presented a problem in therapy and judgment. The dermatologist knew that he would soon be asked whether this soldier could proceed with his unit, and time was of more than the usual importance. Because of this, every soldier was inspected by medical officers immediately on arrival and again forty-eight hours prior to departure. On this second inspection the officers frequently discovered dermatoses previously mild and recently aggravated and reported the patients for treatment just as the unit was preparing to depart. At this point it was the responsibility of the medical officer to the service to send all possible men with their units. It was also his duty to the man and his profession, however, not to send men who could not undertake the march with full equipment to the train, then to the ferry and from the ferry to the transport. In addition to the dermatologic problem present, the man's grade and importance to his unit had to be considered. It was many times more difficult to replace a trained technical sergeant than to replace a private. It was encouraging to see the morale of the units at the staging area station hospital just prior to departure to a combat area, when although the number

of men withdrawn was comparatively small most of them pleaded to be allowed to proceed with their units, despite severe diseases of the skin

The dermatoses most commonly seen were chiefly of six types (table 1) The first six groups accounted for two thirds of all the patients hospitalized Prior to Dec 1, 1944, 723 patients with scabies were hospitalized, but since then there have been only 27 admitted to the hospital The 1,200 patients with scabies seen in the clinic since then have been treated on an ambulatory status This means that although the census since December 1944 may have been smaller it was made up of patients with severe dermatoses

TABLE 1—*Total Number of Hospitalized Patients with Commonest Dermatoses and Percentage of Total Number of Hospitalized Patients with Dermatoses*

Dermatoses	Patients	
	Total No Hospitalized	Per Cent of Total No Hospitalized with Dermatoses
Scabies	750	25.3
Dermatophytoses, all types	488	16.4
Dermatitis venenata, all causes	333	11.0
Dermatitis, unclassified	188	6.3
Impetigo contagiosa	156	5.2
Dermatitis, eczematoid	133	4.4
Intertrigo, axilla or groin	79	2.6
Dermatitis, impetiginous	75	2.5
Urticaria, cause undetermined	65	2.2
Folliculitis, pustular	63	2.1
Dermatitis medicamentosa	51	1.7
Furunculosis	41	1.4
Dermatitis, allergic	39	1.3
Lichen simplex chronicus	32	1.0
Total	2498	83.4

In table 1 one notes that fourteen diagnoses made up 83.4 per cent of all dermatologic diseases of the patients admitted The remaining 16.6 per cent comprised small numbers of the rarer diseases, such as the herpetiform and exfoliative dermatoses, ecthyma, epidermolysis bullosa, ichthyosis congenita, lupus erythematosus, molluscum contagiosum and keratosis punctata palmaris et plantaris, and also a few of the commoner diseases of patients who were admitted at night without the dermatologist's consultation, such as pityriasis rosea, psoriasis, herpes zoster and herpes simplex

The admission of persons with certain types of dermatoses was almost routine No one would hesitate to admit a person with severely infected dermatophytosis pedis or disseminated impetigo On the other hand, the close living conditions and the inability of the men to carry out certain treatments in their barracks made admission obligatory for many men who in civilian life would ordinarily have been treated on an ambulatory status For instance, a soldier had to be hospitalized

when he was unable to shave, when his face was covered with a white or black ointment or when a strong-smelling medicament, such as coal tar or sulfur, was used over a large area of his skin. Hospitalization was also necessary when wet dressings or frequent soaks were prescribed, since neither the time nor the facilities existed in the barracks for this type of treatment.

TABLE 2—Total Number of Patients with Commonest Dermatoses Discharged and Percentage of Total with that Disease and of Total Discharged

Dermatoses	Total No	% of Patients with Disease	% of Total Discharged
Lichen simplex chronicus	10	33.3	22.2
Dermatitis, unclassified	5	2.6	11.1
Dermatophytosis	5	1.0	11.1
Ichthyosis congenita	3	33.3	6.6
Dermatitis, seborrheic	3	37.5	6.6
Dermatitis, exfoliative	3	37.5	6.6
Dermatitis, allergic, due to wool	3	7.7	6.6
Urticaria, cause undetermined	2	3.1	4.4
Dermatitis, impetiginous	2	2.6	4.4
Dermatitis venenata, due to mercury	2	0.6	4.4
Other dermatoses, one each	7		16.0
Total	45		100.0

During the period from June 1942 to September 1945, 45 soldiers received medical discharges from the army because of a dermatologic ailment (table 2), and 116 failed to respond to therapy or presented such severe or widespread dermatoses that they could not be returned to duty in the sixty days allowed for treatment in a station hospital.

TABLE 3—Total Number of Patients with Commonest Dermatoses Transferred to Regional Hospitals and Percentage of Total with Disease and of Total Transferred

Dermatoses	Total No	% of Patients with Disease	% of Total Transferred
Dermatitis, eczematoid	31	23.3	26.7
Dermatitis, unclassified	24	12.8	20.7
Dermatophytosis	24	4.9	20.7
Dermatitis, impetiginous	9	12.0	7.8
Acne vulgaris	4	44.4	3.4
Dermatitis, pustular	4	19.0	3.4
Folliculitis, pustular	3	4.8	2.6
Sycosis vulgaris	3	16.7	2.6
Toxic erythema	2	33.3	1.7
Dermatitis herpetiformis	2	13.3	1.7
Impetigo contagiosa	2	1.3	1.7
Other dermatoses, one each	8		7.0
Total	116		100.0

These were transferred to the designated regional hospitals for further observation and treatment (table 3). The chief disabling dermatologic diseases were dermatophytosis, eczematoid dermatitis and the unclassified dermatoses. These were found in 79 of the 116 transferred patients.

The 2 men who received medical discharges noted under dermatitis venenata were sensitive to mercury, present in the smoke resulting from the explosion of the percussion caps of cartridges and shells. The 3 men discharged with the diagnosis of allergic dermatitis were soldiers allergic to wool who could not be utilized in warmer climates where sun tan cotton uniforms were worn the year round.

The greatest therapeutic problem presented to the dermatologist in this staging area, as may be noted from table 1, was that of the dermatophytoses. There were 488 patients whose lower extremities chiefly were involved. This was 16.4 per cent of all patients hospitalized for dermatoses. Five patients with chronic and recurrent eruptions were given medical discharges while 24 were transferred to authorized regional hospitals. The results of treatment of persons previously hospitalized were discouraging. It was found that unless they were hospitalized early on the initial outbreak and given an adequate period of rest followed by a gradual return to full duty many had relapses almost immediately. To keep a soldier on duty with more than a mild dermatophytosis pedis was to invite a severe infection, possibly with a complicating dermatophytid of the hands and the development of a chronic eruption requiring many months to heal, if healing were to result at all. In general, the dermatologist has found that early hospitalization with rest in bed plus mild therapy was the treatment of choice and in the long run saved days of hospitalization in the management of this infection.

Another problem of general interest was that of the 133 soldiers with eczematoid dermatitis of the extremities. Among these cases, many eruptions of atopic origin were seen. Also, of this group, 10 men with complicating lichen simplex chronicus were discharged and 31 were transferred to regional hospitals. These, as may be noted from tables 1 and 2, head both lists. The neurogenic factors involved in this dermatitis have been recognized, and the army with its discipline and regimentation plus the idea of impending combat did much to aggravate the tendency toward this disease or the existing disease itself. It should be noted that of the 133 soldiers with eczematoid dermatitis 41 were not returned to duty within sixty days and ten of these were given medical discharges.

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## KAPOSI'S VARICELLIFORM ERUPTION

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SINCE 1941 increased attention has been given to the cause of Kaposi's varicelliform eruption. Esser<sup>1</sup> and Seidenberg<sup>2</sup> in 1941 first contributed evidence that the virus of herpes simplex causes Kaposi's varicelliform eruption in at least some cases. Dermatologic attention has not previously been called to the publication by Esser, who described a small epidemic of this disease in an infants' ward, where 4 children became severely ill, 1 dying as a result of the infection. In 2 of Esser's cases the herpetic virus was recovered and identified by Seidenberg. Other investigators have since published reports of cases in which there has been suggestive or conclusive evidence incriminating the herpetic virus. Conditions of war kept the earlier reports from general attention of American dermatologists, but Barton and Brunsting<sup>3</sup> soon described the results of experimental studies in 2 cases of Kaposi's varicelliform eruption. At about the same time, Lynch observed the first of a series of cases in which clinical observation associated the herpetic virus with certain unusual eruptions. At a meeting in April 1944 he reported demonstration of the herpetic virus in a case in which the severity and extent of the eruption were not so great as is usual in Kaposi's disease.<sup>4</sup> Wenner, in April 1944, reported a case in a pediatric journal.<sup>5</sup> Lane and Herold subsequently observed a case of the disease in which Blattner,

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1 Esser, M. Ueber eine kleine Epidemie von Pustulosis varioliformis acuta, *Ann pædiat* **157** 156, 1941.

2 Seidenberg, S. Zur Aetiologie der Pustulosis vacciniiformis acuta, *Schweiz Ztschr f Path u Bakt* **4** 398, 1941.

3 (a) Barton, R. L., and Brunsting, L. A. Kaposi's Varicelliform Eruption. Report of Case, *Proc Staff Meet, Mayo Clin* **18** 199 (June 30) 1943. (b) Kaposi's Varicelliform Eruption, *Arch Dermat & Syph* **50** 99 (Aug) 1944.

4 Lynch, F. W. Herpes Simplex as a Complication of Eczema, paper read at the meeting of the Ramsey County Medical Society, April 24, 1944.

5 Wenner, H. A. Complications of Infantile Eczema Caused by the Virus of Herpes Simplex, *Am J Dis Child* **67** 247 (April) 1944.

Heys and Harrison<sup>6</sup> had demonstrated the presence of herpetic virus. In discussing Lynch's presentation<sup>7</sup> at the 1944 meeting of the American Medical Association, Ebert<sup>8</sup> reported that he had demonstrated inclusion bodies typical of the herpes group of diseases and had produced keratitis in a rabbit's eye. At about the same time Lane<sup>9</sup> discussed the subject before the American Dermatological Association and presented excellent photographic representation of several cases of the disorder.

The present report deals with 4 additional cases of extensive or disseminated herpetic eruptions, in but 1 of which the course and symptoms



Fig 1—Kaposi's varicelliform eruption (case 5) with labial herpes simplex which preceded the extensive facial eruption

were as severe as those usually associated with the condition in the title, Kaposi's varicelliform eruption.

CASE 5—D. S. (fig 1), a man aged 23 years, had had extensive eczema since birth. In recent years it had been present principally on the face, in the cubital areas and on the forearms and hands, at certain times it was dry, and at other times it was exudative.

On March 15 labial herpes simplex developed, on March 17 the eruption extended near the left eye, and it continued to spread until March 20, after which the eruption became severer but without development of additional lesions.

6 Blattner, R. J., Heys, F. M., and Harrison, M. A Filterable Virus Isolated from a Case of Kaposi's Varicelliform Eruption, *Science* **99** 432 (May 26) 1944.

7 Lynch, F. W. Kaposi's Varicelliform Eruption. Extensive Herpes Simplex as a Complication of Eczema, *Arch. Dermat. & Syph.* **51** 129 (Feb.) 1945.

8 Ebert, M. H., in discussion on Lynch.<sup>7</sup>

9 Lane, C. W., and Herold, W. C. Kaposi's Varicelliform Eruption: Report of Five Cases, *Arch. Dermat. & Syph.* **50** 396 (Dec.) 1944.

Examination then revealed about fifty discrete tense vesicles on the right cheek, there were many similar lesions over the left zygoma and on the left cheek. The bases of the lesions were red, and the larger lesions were umbilicated. The left preauricular node and the right and left submaxillary nodes were enlarged. On March 22, the temperature was 99.8 F and the lesions were regressing. On March 24 and 25 he had nausea, malaise, headache and some dizziness. In the next ten days the eruption gradually disappeared, without scar but leaving hyperpigmentation.

On March 20 fluid was obtained from a blister and inoculated on the cornea of a rabbit. At forty-eight hours severe keratoconjunctivitis had developed. After a week there developed in the rabbit paresis of the right legs and a tendency to walk in a circle, falling toward the affected side. On April 6, the rabbit was killed and sections of the brain were stained with hematoxylin and eosin. Scattered through the brain were found small areas of necrosis and round cell infiltration. In these areas the nerve cells showed margination of the nuclear chromatin, and intranuclear, acidophilic inclusion bodies were present.

The appearance and course in this case were characteristic of moderately severe examples of Kaposi's varicelliform eruption. In the 3 following cases, the eruption was much less extensive and the course was mild. In case 6 there were no signs or symptoms of toxicity. These cases are presented for the purpose of pointing out that while Kaposi's varicelliform eruption may be a clinical entity there are undoubtedly many cases in which herpetic eruptions are more extensive than ordinary herpes simplex but less extensive and severe than Kaposi's varicelliform eruption.

CASE 6—A L., a woman aged 20 years, had suffered from extensive chronic eczema for about ten years. After the appearance of labial herpes simplex the new moist and papulovesicular eruption appeared, also in the form of grouped lesions on both upper lids, and subsequently spread on the chin at a distance from the labial eruption. New lesions continued to develop over a period of several days, without evidence of general toxicity. Recovery was prompt.

CASE 7—M K., a patient with extensive facial acne, noted redness and swelling below each ear and burning and itching on the upper lip. On the following day the eruption spread over the face, and for several days the temperature rose to 100 F. When the patient was seen on the fifth day of her illness, the face presented an extensive eruption of single and grouped bright red papules, some papulovesicles and some crusted lesions. The patient felt generally ill. The throat was sore and the left tonsil presented a few small discrete white areas. The white blood cell count was 6,700, and the sedimentation rate of the blood was 44 mm in one hour. On the following day more of the papules transformed to vesicles, but the eruption improved steadily thereafter. The temperature was 99.4 F and 99 F the two succeeding days.

CASE 8—F T A., a man aged 69 years, stated that he had had several attacks of eczema over a period of ten years, but the current outbreak was said to be the severest. There were discrete tense vesicles, vesicopustules and crusted lesions, all with erythematous papular bases. They were in a group on the lateral portion of the left upper lid and eyebrow and were numerous near the left angle of the mouth. On the face they were scattered, more on the left side. There were

a small left preauricular node and a larger left submental node. His temperature was 99.6 F. He was vaccinated with smallpox vaccine, and the facial eruption was improved when he returned two days later but a few discrete, crusted papular lesions had appeared on the hands and ankles. The temperature was then 98 F. Subsequently the eruption healed rapidly, leaving areas of scaling and thickening on the lids, elsewhere on the face and on the neck and wrists, as before the acute eruption.

The report of Barton and Brunsting in 1944 provided a thorough review of previously published data regarding Kaposi's eruption. In the accompanying table we have summarized certain data concerning the recent cases in which herpetic infection has been proved or may reasonably be assumed (table). No important differences are apparent in a contrast of this group with the group reviewed by Barton and Brunsting in which the cause was unknown. This absence of difference suggests that herpetic infection may be the only cause of Kaposi's varicelliform eruption.

#### DIAGNOSIS

In contrast with the reports of laboratory studies by most other authors, the diagnosis of extensive herpes simplex was based on clinical observation in each of the 7 cases reported in our two series. Since the herpetic virus was found and identified in the 2 cases in which proper search was made, there is not much reason to doubt the diagnosis in any case. It is our belief that clinical diagnosis is not difficult if one thinks of the correct possibility. The observer must realize that herpes simplex exists in several forms, one of which is an extensive eruption superimposed on a preceding dermatosis, and that Kaposi's varicelliform eruption is not a particularly satisfactory descriptive term for this disease because not all patients (perhaps only a minority) present such extensive eruptions and general toxemia. Though there may be clinical resemblance to varicella in some cases, the resemblance can be slight and the vesicles can better be described as herpetic. In spite of the greater extent of Kaposi's varicelliform eruption, the diagnosis depends chiefly on recognition of the resemblance to herpes simplex. The inflammatory papules quickly become vesicles which are tense, and some of them are umbilicated. They soon rupture, perhaps because of the acuity of the inflammatory process but also because they are subjected to trauma because of the attempts to relieve the discomfort of the preceding eruption of which the herpetic infection is a complication. The grouping of lesions, so characteristic of herpes simplex, is less striking in this disease but is still evident to careful examination.

With any considerable extent the eruption is accompanied with general symptoms whose severity is greater than one would expect with pyogenic infection of similar extent. There is fever, loss of appetite, lassitude, malaise or even prostration. In the cases of severer condi-

*Summary of Data in Reported Cases of Kaposi's Varicelliform Eruption*

Author	Age of Patient	Sex	Severity	Virus Identified	Contact with Herpes	Herpes Labialis	Preceding Dermatitis
Jancz	1 Infant		Severe *, died	In 2 cases †	Not stated, cases apparently epidemic	Not stated	Infantile eczema all cases
	2 Infant		Severe, recovery				
	3 Infant		Severe, recovery				
	4 Infant		Severe, recovery				
Barton Brunsting	1 30 yr	M	Severe, meningeal symptoms	No	Not stated	No	Atopic eczema
	2 21 yr	F	Mild	Yes	Not stated	Yes	Atopic eczema
Wenner	1 5 mo	F	Died †	Yes	Not stated	Not stated	Infantile eczema
	2 20 mo	M	Severe, recovery	Yes	Not stated		Infantile eczema
	3 8 mo	F	Severe, recovery	Yes	Not stated		Infantile eczema
Lane and Herold	1 20 yr	M	Mild	No	Not stated	No	Neurodermatitis
	2 14 yr	M	Moderate	No	Not stated	No	Eczema
	3 17 yr	F	Moderate	No	Not stated	No	Neurodermatitis
	4 3 yr	F	Severe	No	Not stated	No	Neurodermatitis
	5 15 mo		Severe	Yes	Not stated	No	Large cutaneous eruption
Lynch	1 2½ yr	M	Mild	No	Father	No	Atopic eczema
	2 20 yr	F	Moderate	No	No	Yes	Atopic eczema
	3 10 mo	M	Moderate	No	Mother	No	Infantile eczema
	4 5½ yr	F	Mild	Yes	Possible	No	Atopic eczema
Pbert	1 "Young" woman	F	Severe	Yes	Not stated	No	Not stated
Lynch and Steves	5 23 yr	M	Moderate	Yes	No	Yes	Atopic eczema
	6 20 yr	F	No symptoms	No	No	Yes	Atopic eczema
	7 28 yr	F	Mild	No	No	No	Excoriated acne
	8 69 yr	M	Mild	No	No	No	Atopic eczema

\* Report of autopsy suggested encephalitis

† Seidenberg<sup>2</sup>

‡ Encephalitis with herpetic virus isolated from brain of the infant

tions one is likely to observe signs and symptoms of cerebral involvement. As in many diseases due to viruses the white blood cell count is elevated but not to the degree seen in pyogenic disorders. Neither the general symptoms nor the course of the eruption is greatly influenced by ordinary therapy, including the use of sulfonamide drugs. As with herpes simplex, the inflammation may be slightly relieved by proper topical therapy and the symptoms may be somewhat alleviated, but the eruption pursues a course of five to ten or twelve days, depending on its extent and severity.

The correct diagnosis may be aided somewhat by the history of a preexisting eruption having erosions or excoriations allowing inoculation and spread of the virus. The patient may have ordinary herpes simplex of the lips or eyelids, present for one to several days before the rapid extension of the inflammation. In other cases one may obtain a history of contact or even observe on the patient's attendant evidence of preceding localized herpes simplex.

It is possible that other than herpetic infections can be superimposed on eczematous eruptions producing eruptions like that of Kaposi's disease. It is possible that pyogenic infection can produce a similar eruption.<sup>10</sup> In attempting to confirm a diagnosis of herpetic complication of eczema, one is confronted with certain difficulties. Laboratory investigation of viruses is time consuming, and the facilities are not always or everywhere available. In order to get successful results, one must obtain fluid from an intact vesicle in the first several days of the illness, at a time when the patient may not yet have presented himself for examination. Inoculation of the cornea of a rabbit is the starting point for identification of the virus. However, as shown by Ebert, the inclusion bodies of herpes simplex may be found in histologic sections of the eruption.<sup>8</sup> The development of a keratoconjunctivitis may follow inoculation with viruses of both vaccinia and herpes simplex, making the demonstration of inclusion bodies essential. The diagnosis of herpetic infection is established by the appearance of the acidophilic intranuclear inclusion bodies of herpes simplex in the cornea during the first forty-eight hours or later in the brain. Immunologic studies are difficult and usually unnecessary, and the presence of antibodies against herpes simplex virus in human blood serum is subject to great variation.

It is our opinion that the demonstration of herpetic inclusion bodies, in the lesion itself, in the cornea of the rabbit soon after inoculation or in the brain after encephalitis develops, is the most expedient and reliable method of establishing a herpetic causation (figs 2 and 3).

10 McLachlan, A. D., and Gillespie, M. Kaposi's Varicelliform Eruption Epidemic of Sixteen Cases, *Brit J Dermat* 48:337 (July) 1936.



Fig 2—Section from a rabbit's brain after the cornea was inoculated with herpetic virus. There are three areas of necrosis and cellular infiltration. It is in areas like this that one finds inclusion bodies such as are demonstrated in figure 3.  $\times 90$

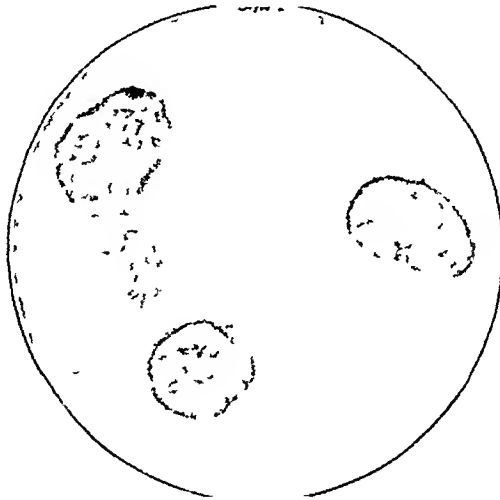


Fig 3—Drawing of changes observed in a single microscopic field from the brain of a rabbit whose cornea had been inoculated with herpetic virus. In the three neurons on the left are seen intranuclear herpetic inclusions in various stages of development. In the cell on the right there is margination of chromatin, which is a constant finding in herpetic infection.

## EPIDEMIOLOGY

It has sometimes but not always been possible to determine the source of herpetic infection in Kaposi's varicelliform eruption. Esser reported a small epidemic, implying the presence of contagion from child to child, but it is possible that the source in each case may have been a nurse or other attendant suffering from herpetic infection. Such a method of inoculation was reported in cases 1 and 3 of the first series reported by Lynch.<sup>7</sup> In the first instance a child was exposed to his father, who had herpetic infection of the eyelid, and in the third case an infant was exposed to his mother, with labial herpes. In case 4 the source of infection may have been the attending physician. Apparently autogenous inoculation also occurs. Thus in case 6 of our present series and in case 2 previously reported, the onset of the varicelliform eruption was preceded for two days by labial herpes. In 1 case reported by Barton and Brunsting the extensive eruption was preceded by localized herpes simplex.<sup>8</sup> In discussing the paper by Lane and Herold, Lynch pointed out that the lantern slides of the photographs showed suggestive evidence that localized herpes simplex had occurred on the upper eyelid in cases 1 and 3, because lesions were further advanced and grouped more closely than elsewhere (see particularly figure 3 in their publication).<sup>9</sup>

## TREATMENT

In ordinary cases of Kaposi's varicelliform eruption there is little to be done in addition to reasonable use of topical measures according to the usual dermatologic principles. In cases of severe eruption with progressive toxemia and evidence of involvement of the central nervous system, one should consider the use of serum therapy, as suggested by Evans, Bolin and Steves.<sup>11</sup>

## TERMINOLOGY

Terminology deserves brief discussion in the light of both etiologic and clinical advances in recent years, which make possible a more satisfactory classification and nomenclature. In discussion of the suggested titles "eczema herpeticum" and "extensive herpes simplex complicating eczema (or other dermatoses)," Sulzberger suggested that the disease be spoken of as "disseminated herpes simplex" or "Kaposi's form of herpes simplex."<sup>12</sup> Kaposi himself suggested "eczema herpetiforme."<sup>13</sup> In a related disease, vaccinia, one speaks of multiple vac-

11 Evans, C. A., Bolin, V. S., and Steves, R. J. Kaposi's Varicelliform Eruption. Addendum. Experimental Data with Suggested Therapeutic Application. *Arch Dermat & Syph* **51** 134 (Feb) 1945.

12 Sulzberger, M. B., in discussion on Lynch.<sup>7</sup>

13 Kaposi, A. Pathology and Treatment of Diseases of the Skin, ed. 4, translated by J. C. Johnston, New York, William Wood & Company, 1895, p. 346.

cima in cases of less extensive eruptions, but when the eruption is more extensive, is superimposed on eczema and results in severe toxemia one uses the term "eczema vaccinatum." Similar wording in cases of herpetic infections would utilize the term "Kaposi's eczema herpeticum," mention of varicella being avoided, whose virus is not concerned in the disease.

If all eruptions can be called herpetic when caused by the virus of herpes simplex, there are then two main groups of cases, the first are those in which the virus exerts its influence on previously apparently intact skin. The eruptions may vary in site and extent but are clinically closely comparable. Herpes simplex may be (a) localized herpes



Fig. 4—Herpes simplex which is more extensive than usual but still localized

simplex (the site, i. e., labial, genital, aural or ocular being specified) or (b) extensive herpes simplex, in which the eruption is of greater than usual extent, presenting as a single group of lesions or with the addition of smaller groups or single lesions nearby.

Lutz<sup>14</sup> described 2 cases of this type of eruption, under the name 'acute vacciniiform or varioliiform pustulosis.' Figure 4 presents a somewhat comparable eruption but without satellite lesions. In Lutz's cases the vesicles were more widely distributed, though limited to the face and the lesions were more discrete.

14 Lutz, W. Ueber Pustulosis vacciniiformis sive varioliiformis acuta. *Dermatologica* 86 138, 1942.

More extensive eruptions may follow the exposure of nonintact skin to herpetic virus. The extent of the eruption and the severity of the illness are chiefly dependent on the nature and extent of the preceding eruption and the age of the patient. The preceding eruption is not always eczema.

Herpetic inoculation as a complication of another dermatosis may be either (*a*) mild, but with the eruption usually of greater extent than in extensive herpes simplex (*b* in foregoing classification) and scattered in distribution, or (*b*) severe (Kaposi's varicelliform eruption, Kaposi's herpetiform eruption or eczema herpeticum).

#### SUMMARY

The purposes of this presentation have been two. First, we have reported an additional instance of the demonstration of the virus of herpes simplex in Kaposi's varicelliform eruption. Second, we have described several additional examples of disseminated herpetic infection occurring with clinical manifestations less severe than Kaposi's varicelliform eruption but severer and more extensive than those usually noted in herpes simplex (in the second classification presented). Whether or not one chooses to use these terms, it will be well to remember that there are variations in the clinical features of herpes simplex, from the mild disease characterized by several small papulovesicles to a severe, generalized eruption accompanied with systemic infection and possibly fatal termination.

## DERMATOPHYTOSIS OF THE FACE CAUSED BY TRICHOPHYTON CAMEROUNENSE

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THE FOLLOWING case of dermatophytosis of the face seems worthy of publication, since the causative fungus presented features that rendered its detection difficult enough for one to assume that the true nature of similar cases may have been overlooked. The fungus involved, *Trichophyton* (*Grubyella*) *camerounense* (Ota and Gaillard 1926), has been recovered only once. It was found in the mycotic lesions of a bull transported from Cameroun, West Africa, to Paris, France, for studies in tropical piroplasmoses<sup>1</sup>. Unknown as yet has been its occurrence in America and its pathogenicity to human beings.

### REPORT OF A CASE

A white boy, 14 years old, complained of red spots on his face that had appeared three months previously on the right cheek. They had spread to the neck and to the left eye and had been slightly itchy.

On examination, nearly the entire right cheek presented a red, round area that when seen from a distance seemed to be a healthy red cheek. At closer inspection, however, the red area as a whole was seen to be slightly elevated above the level of the normal skin. It was covered by a thin scabiness, comparable to chapped skin caused by rough weather. There was no clearing in the center. The border of the area was well defined but was in no way different from other portions of the lesion. A similar but smaller area, of oval shape, was seen on the skin covering the right lower rim of the mandible. A third lesion filled the left sulcus infrapalpebralis.

A scraping was taken from the border of the largest lesion. Microscopic specimens prepared with a solution of potassium hydroxide revealed only a few mycelial threads about 2 microns in diameter, which failed to show the sharply defined refraction rarely lacking in the hyphae of the genus *Trichophyton*. When stained with a 0.5 per cent solution of cotton blue C4 in lacto-phenol, however, the specimen presented numerous, large, nearly round spores, measuring up to 14 microns in diameter (figure, a).

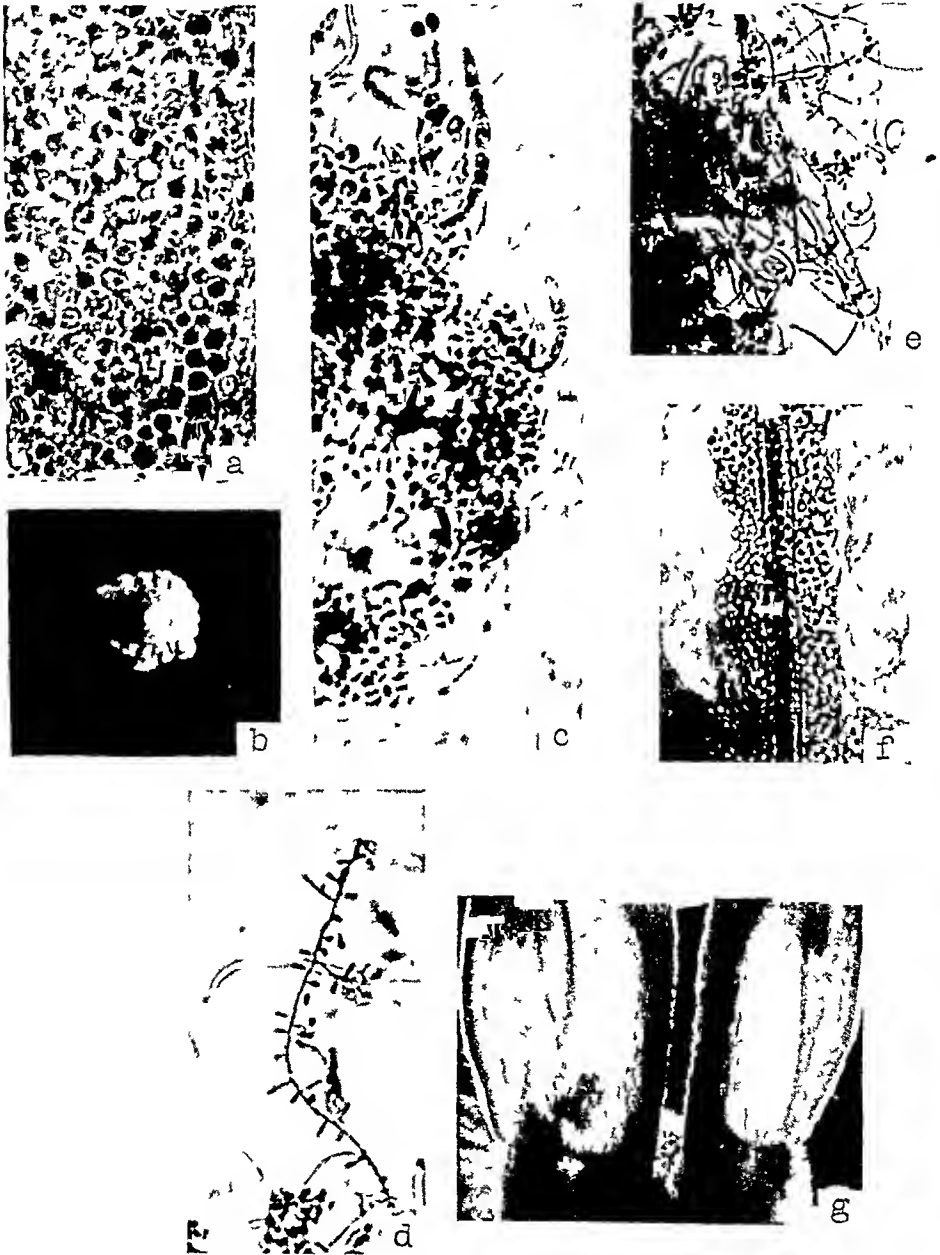
Glucose-peptone slants inoculated from the scraping developed several colonies of cocci. At the end of four weeks, there became visible three colonies, of pin-

Dr Bernhardt died Feb 27, 1946

From the Department of Dermatology and Syphilology (Dr John Godwin Downing), Boston City Hospital

1 Ota, M. Sur une teigne trichophytique d'un bovidé du Cameroun produite par une espèce nouvelle de *Grubyella*, *G. camerounensis* N. Sp., Ann de parasitol 4 14-21, 1926

head size and shape, that were covered with a short, velvety aerial growth. Subcultures on peptone agar developed faster presenting an elevated, white, powdery center and irregular, colorless, submersed rays. On transfer to a medium composed of 2 per cent maltose, 8 per cent glucose and 1 per cent Fairchild peptone



(a) Chlamydospores in scraping from skin, (b) seven weeks' old subculture on test medium (1:1), (c) fuseaux from rice culture, (d) aleurospore from corn meal agar, (e) spirals from corn meal agar, (f) rabbit hair surrounded by large spores, (g) lesion on left ear lobe of rabbit seven weeks after inoculation (All microscopic specimens were stained with cotton blue in lacto-phenol)

agar, a hemispheric colony developed. This medium, when Weidman's researches<sup>2</sup> are taken into account, with available American ingredients resembles as closely as possible Sabouraud's original test medium. After four weeks at room temperature the hemisphere was 8 mm in diameter and 4 mm high and was covered with a slightly brownish, velvety growth. After another week it was surrounded with a ring, lighter in color, 3.5 mm broad and 1.5 mm high. This ring presented sixteen radial furrows between sectors that slanted to them and to their rounded peripheral ends. The center of the colony resembled the protruding disk of some flowers, such as certain asters, pyrethrums and chrysanthemums, and the surrounding sectors resembled the petals of these flowers. After two more weeks, a fluffy aerial growth appeared on two spots of the periphery (figure, *b*). This disappeared in the following weeks, however, being replaced by an irregular and more furrowed extension of the colony. Repeated subcultures on the same medium also developed hemispheres, which progressed, however, to approximate the shapes of *Trichophyton*, described as plicatile, papillose, verrucose and floriform, except for the difference in color, which was a shade of brown or, rarely, white.

Hanging block and hanging drop cultures in peptone, with or without maltose or glucose, present as main features pediculate and intercalary chlamydospores. Corkscrew-like hyphae were also seen in liquid medium. On rice medium there developed aleurospores (2 by 4 microns) on simple, rarely on compound, thyrsi, as well as fuseaux (up to 4 by 41 microns), with up to six compartments (figure, *c*), and chlamydospores. On corn meal agar there developed aleurospores, chlamydospores and spirals (figure, *d* and *e*). The wall of the hyphae as well as the wall of the chlamydospores failed to take the stain (cotton blue). Within the hyphae, well stained rectangular bodies were visible. As soon as chlamydospores became abundant, poorly stained filaments and unstained chlamydospores became numerous. Fuseau-like chlamydospores were occasionally seen, but fuseaux of the type seen in rice cultures were never observed to change to chlamydospores.

The original scraping was kept between slides at room temperature. Portions of it were inoculated on culture medium after several months. Primary colonies developed from a three month and a six month old inoculum. The colonies appeared in some instances after two weeks. Their shape on glucose-peptone agar was always hemispheric.

*Animal Inoculations*.—On the inoculated ear lobe of a rabbit there appeared after three weeks a scaly lesion, which changed during the following weeks to a crusty, elevated, round area (figure, *g*). Microscopically, the scales contained sporulated filaments. At the time the crusts formed, most of the hair follicles were filled with large spores (up to 4.5 microns in diameter), which surrounded the hairs (figure, *f*). Although numerous specimens were examined, not a single hair was found to be invaded by fungous elements. The lesion healed after seven weeks. The other ear lobe was then inoculated as well as the ear lobe of another rabbit formerly inoculated with *Trichophyton mentagrophytes*, var. *asteroides*. Both inoculations developed in a similar manner to the lesion shown

2. (a) Weidman, F. D., and McMillan, T. M. A Comparison of Ingredients of Ringworm Culture Mediums with Special Reference to American and French Crude Maltose, *Arch. Dermat. & Syph.* 4: 451-468 (Oct.) 1921. (b) Weidman, F. D., and Spring, D. A Comparison of Ringworm Culture Ingredients, *ibid.* 18: 829-851 (Dec.) 1928.

in the figure, *g* A guinea pig that was inoculated died of an unknown cause after sixteen days, sections of the skin showed hyphae invading the hair follicle. The same kind of fungus was recovered by culture from the scales and crusts of every animal inoculated.

*Etiology*—The patient frequented a railroad yard to play with cattle that were fenced in there before being taken to the slaughterhouse. The patient's sisters, who did not visit the cattle yard, did not become infected.

*Therapy*—The first treatment consisted of the application of ointment of benzoic and salicylic acid prepared with Aquaphor. This ointment proved irritating to the eye, and the lesion near it was therefore treated with an ointment containing 1 per cent yellow mercuric oxide. It improved faster than the other lesions, which were then treated with diluted tincture of iodine. Improvement remained incomplete until all the lesions were treated with 2 per cent yellow mercuric oxide in Aquaphor. Thereafter they cleared up rapidly.

#### COMMENT

*Tinea circinata* is a term designating ringlike lesions. Since there was no central clearing in this case, the term dermatophytosis seems more appropriate.

The true nature of the disease might have been overlooked by routine methods, since there were only a few indistinct mycelial filaments to be found, not to mention the slow development and smallness of the colonies on culture medium. The irregular mass of chlamydospores in the native specimen could not be distinguished from other cell material until it had been stained. The development of colonies of cocci on the routine slants rendered improbable the later appearance of fungus colonies, the nature of which became visible only on scrupulous inspection.

Microscopic examination of mounts from different mediums revealing aleurospores, fuseaux and spirals establishes the fungus involved as a *Trichophyton*. The spores surrounding the hair identify it as an ectothrix. Their large size justifies the classification as a megaspore. Sabouraud reported three species of faviform fungi among the megasporic *Ectotrichophyton*s. The fungus described in this paper resembles these species so far as its colonies are slow growing, covered only with a minute velvet and showing nearly exclusively chlamydospores when grown on Sabouraud's medium. The hemispheric form of the colony up to four weeks is the main difference, if one does not consider the large number of chlamydospores in the cutaneous scraping and the aleurospores, fuseaux and spirals revealed on mediums that were hoped for but not used by Sabouraud.<sup>3</sup> A review of the literature failed to reveal a fungus with exactly the same description. There is only one *Trichophyton* presenting similarities enough to assume that it belongs to the same species. It is *Grubyella camerounensis* (Ota and Galliard,

3 Sabouraud, R. *Les teignes*, Paris, Masson & Cie, 1910, p. 652.

1926), renamed *Trichophyton papillosum* by Lebasque in 1933<sup>4</sup> and *Favotrichophyton camerounense* by Dodge<sup>5</sup>. There is the same small size of the colony on a medium containing glucose and peptone, the same hemispheric shape of the early colony, later on sometimes surrounded by a folded periphery, and the same prevalence of chlamydospores on Sabouraud's medium. The differences are not striking enough to justify establishment of a new species, although the name *Trichophyton hemisphericum* seems more appropriate in view of the shape of the early colony on a medium containing glucose or maltose.

The inoculations of animals show that the fungus is pathogenic, at least to rabbits and guinea pigs. The slow development of the experimental lesions and their long persistence are in contrast to results of inoculations with most of the trichophytins, as the resulting lesions usually appear during the second week and vanish during the third week.

#### SUMMARY

An unusual mycosis of the face and its causative organism, *Favotrichophyton camerounense*, are described. This is the second isolation of this fungus, the first one in America and the first from a human lesion. Difficulties in its detection are mentioned. An ointment containing 2 per cent yellow mercuric oxide in Aquaphor seems to be curative.

<sup>4</sup> Lebasque, J. Les champignons des teignes du cheval et des bovidés, Thesis, University of Paris, 1933, pp 71-77.

<sup>5</sup> Dodge, C. W. Medical Mycology, St. Louis, C. V. Mosby Company, 1935, pp 515-517.

## GRANULOMA INGUINALE INVOLVING BUTTOCK AND LYMPH NODE

Cultivation of the Donovan Body in Embryonic Yolk

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THE FOLLOWING instance of granuloma inguinale is reported because of the unusual clinical history, involvement of the lymphatic system and establishment of the etiologic agent by means of cultivation in embryonated eggs

### REPORT OF A CASE

*Clinical Course*—A 20 year old Negro was admitted Jan 6, 1945, complaining of a "sore near my rectum" Approximately four weeks before admission he first noted a painful pimple on his left buttock It rapidly increased in size so that within three days he was unable to continue his work as a checker of cargo that was being unloaded on the beaches of Leyte, Philippine Islands The pimple ruptured on the fourth day and drained a considerable amount of pus, which relieved the pain Copious amounts of pus drained during the ensuing week, the lesion increased in size, and he was admitted to a station hospital There with the patient under pentothal sodium anesthesia an incision was made, with the release of a considerable amount of pus A diagnosis of ischiorectal abscess was made, and two weeks later he was transferred to another station hospital, because the lesion was increasing in size, tender, indurated and had a foul discharge He was later transferred to this general hospital for further treatment

The previous history of this patient is of interest in that he was admitted to a general hospital Feb 10, 1944, almost one year before this admission, because he was allegedly involved in homosexual practices, notably sodomy Examination, including rectal smears, revealed no abnormality, and repeated questioning failed to elicit a confirming admission from the patient The history further indicated that after discharge from the hospital he was the only one of several men in his unit who was not declared guilty of homosexual practices by a General Court Martial

He admitted frequently visiting houses of prostitution in Honolulu, Territory of Hawaii, during the summer of 1944 but stated that he definitely did not have sexual contact after September, when he sailed for Leyte The patient stated that he had never had a lesion on his penis

Examination of this asthenic and acutely ill Negro revealed nothing remarkable except that on the left buttock adjacent to the anal orifice, in the 9 o'clock position, there was an indurated and undermined area about 5 cm in diameter containing

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several fistulas that drained a foul purulent fluid and necrotic tissue. A similar area about 2 cm in diameter was seen in the 11 o'clock position. Surrounding these areas for a distance of 2 to 4 cm there was a moderately tender zone of induration. On the right buttock in the 2 o'clock position there was an area of induration about 5 cm in diameter with three tiny fistulas near its anal margin. There was no lesion on the genitals. The inguinal lymph nodes were not enlarged or tender.

On admission the patient's immediate difficulty was interpreted as being due to an incompletely drained abscess. Incision and drainage were done Jan 6, 1945, and biopsy specimens taken. It was found that immediately beneath the areas noted on the left buttock, the partially necrotic skin was entirely undermined by sloughing necrotic subcutaneous tissue. The sinuses of the two areas noted on the left buttock converged subcutaneously and led into an abscess cavity along the right side of the anus and rectum which was about 11 cm deep and contained thick creamy pus. No pustules or sinuses were demonstrated to extend into the area of induration that surrounded this abscess cavity.



Fig 1—Appearance of lesions on Feb 9, 1945, before treatment with fuadin. Dark line indicates the area of induration.

The patient was given penicillin, 25,000 units every three hours, and hot compresses. The drainage gradually decreased and became less foul and purulent. The necrotic tissue sloughed away, including the bridge of skin between the two lesions of the left buttock. During a period of three weeks the appearance of the lesion became different from that found on admission. It suggested a granulomatous process composed of spongy red moist granulation tissue. The advancing elevated, well defined, serpiginous border tended to roll over on the bordering skin (fig 1). Also during this period a lymph node in the right inguinal region became definitely enlarged, but it was not tender.

The smear and culture taken on admission were negative. The biopsy showed acute and chronic inflammation with epithelial hyperplasia. The diagnosis was in doubt, so on January 29 the enlarged right inguinal lymph node was excised. Further biopsies and smears were taken of the lesion on the left buttock. The

report from these smears and biopsies established a diagnosis of granuloma inguinale

On February 14 the first course of fuadin (sodium antimony III bis-catechol-2, 4 disulfonate) was started. The initial dose was 1.5 cc, followed in two days by 3.5 cc, and thereafter 5 cc was given twice weekly for a total of 45 cc. A second course of fuadin was started on March 17. A third course was started on April 24, and the dosage increased to 5 cc of fuadin every other day. At no time were toxic symptoms observed.

During this course of treatment with fuadin there was a gradual and definite improvement of the lesion. The foul discharge almost ceased, and the surface became covered with clean firm granulation tissue. The edges became level with the adjacent skin, and definite epithelization of the edges that was almost free of pigmentation was seen. The area of induration had decreased approximately 60 per cent (fig 2). After three weeks of treatment the patient ceased to be bedridden, and thereafter he showed great improvement. On May 4 he was placed on orders for evacuation to the mainland.



Fig 2—Appearance of lesion on April 23, 1945, after treatment with 90 cc of fuadin

The blood cell count on admission January 6, was 3,670,000 red blood cells, hemoglobin 75 per cent, white blood cells 19,950, with 78 per cent neutrophils, 20 per cent lymphocytes and 2 per cent monocytes. Numerous blood counts during his stay in this hospital showed a gradual decrease in the white blood cell count and an increase in red blood cell count. On April 9 the blood cell count was 4,390,000 red blood cells, hemoglobin 90 per cent, white blood cells 7,300, with 38 per cent lymphocytes, 59 per cent neutrophils and 3 per cent eosinophils. The sedimentation rate (determined by the Westergren method) dropped progressively from 108 mm per hour on February 3 to 54 mm per hour on April 29. The blood chemistry report on February 9 showed a total protein of 7.2 Gm, albumin 3.8 Gm and globulin 3.4 Gm, giving an albumin-globulin ratio of 1.1. The formaldehyde-gel test showed a semigel in three hours. Repeated blood chemical determinations on February 26 and on April 9 showed no appreciable variation from these figures. Cultures taken January 6, January 22, January 23 and February 5

from the lesion on the buttock showed no growth, but one taken on February 2 showed scattered colonies of diphtheroids. Smears done on January 6 and February 2 showed no organisms, but on February 6 a smear demonstrated the presence of Donovan bodies. The Kahn and Wassermann reactions were negative on January 6, February 7, February 9 and April 26. On examination of the feces on February 8 and February 16, no occult blood, parasites or ova were found. Reactions to Frei tests on February 6 and February 12 were negative. Complement fixations with a lymphogranuloma venereum antigen on February 9 and April 26 both showed a reaction of 4 plus with an initial dilution of serum of 1:20.

*Pathologic Examination*—One part of the gross specimen consisted of two masses of tissue measuring 3.4 by 1.3 by 1.2 cm and 1.5 by 1 by 0.9 cm. Each mass of tissue was partially covered with dark skin. Along one margin the

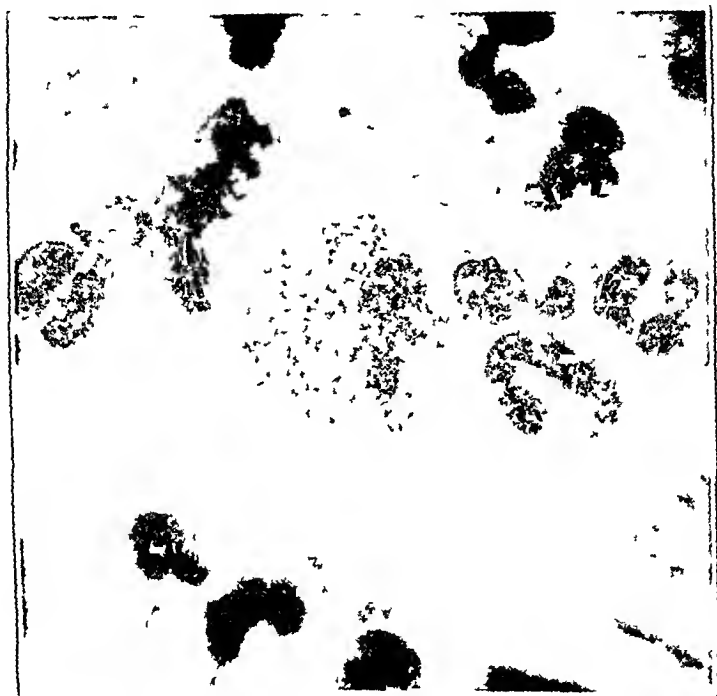


Fig 3—Mononuclear cell with intracellular Donovan bodies. Touch smear of ulcer of patient. Wright's stain,  $\times 1,200$ .

skin was rolled and pale. The contiguous surface was ulcerated, irregularly granular and mottled red and yellow. The cut surface beneath the intact skin appeared as gray normal subcutaneous tissue. Beneath the ulcerated zone the cut surface was slightly translucent and gray-yellow with scattered hemorrhagic foci.

The second part of the specimen consisted of a lobular mass of tissue measuring 3.5 by 2.7 by 2.5 cm. The external surface was gray-pink with adherent bits of fibrous tissue. The cut section disclosed the outlines of two lymph nodes, the surface of which was gray-pink, congested and marked by small gray opaque foci.

The tissues were fixed in a solution of 10 per cent formaldehyde. Paraffin sections were prepared and stained with hematoxylin and eosin stains and Giemsa stain and by the silver impregnation method of Dieterle. In addition, touch smears were prepared from the tissue at the site of the ulcer and stained with Giemsa stain and with Wright's stain.

The cellular content of the touch smears was comprised predominantly of leukocytes but included many large mononuclear cells. The mononuclear cells generally contained many Donovan micro-organisms, which were frequently bacillary in shape with bipolar concentrations of chromatin and a well defined capsule (fig 3).

For microscopic examination sections of tissue were selected to include the intact skin and the ulcerated zone. In general, all except the superficial layers of the skin contained pigment. There was a slight hyperkeratosis, and the rete pegs were frequently elongated and sometimes branching. The cutis showed edema of the interpapillary and subpapillary zones. Blood vessels and the skin appendages were surrounded by tenuous edematous stroma, and the perivascular stroma was infiltrated with inflammatory cells which were mostly plasma cells. There were several mast cells scattered throughout the stroma and near blood vessels. At the margin of the ulceration, slightly pigmented squamous epithelium extended irregularly into the underlying stroma.



Fig 4—Mononuclear cells with intracellular Donovan bodies and vacuolated cytoplasm. Histologic section of ulcer of patient. Hematoxylin and eosin,  $\times 1,500$ .

The base of the ulceration was composed of a luxuriant richly vascularized granulation tissue. The stroma between the capillaries was scanty, edematous and highly infiltrated with inflammatory cells and scattered collections of red blood cells. The exudate was often rich in polymorphonuclear leukocytes. In addition, there were lymphocytes, plasma cells and a number of mononuclear cells, particularly in the superficial zone, filled with minute bacillary bodies. In some instances the bacillary forms were situated in a vacuolated cytoplasm, and occasionally they were encountered outside of the cell (fig 4).

On microscopic examination the general architecture of the lymph node was intact. There were a few small foci of fibrosis. The primary and secondary nodules were moderately prominent. The blood vessels throughout the node were dilated and hyperemic. Likewise, the peripheral lymph sinuses and to a slight

lesser degree the central sinuses were dilated. The peripheral sinuses were often filled with lymphocytes, plasma cells, monocytes and a few polymorphonuclear leukocytes. Situated within the lymph sinuses were rare mononuclear cells containing minute bacillary bodies (fig 5). The capsule in places was thickened by fibroblastic proliferation accompanied by a moderately heavy infiltration of cells, chiefly plasma cells and lymphocytes (fig 6). Occasionally mast cells were encountered in the capsule and within the node.

*Experiments*—On February 9 and again on February 15, specimens for biopsy were taken near the skin margin, and saline suspensions of the ground granulation tissue were inoculated into the yolks of embryonic chicks. On both occasions, an organism was isolated which resembled *Donovania granulomatis* as described by Anderson, De Monbreun and Goodpasture,<sup>1</sup> and on both occasions a passage strain was established.



Fig 5—Mononuclear cell with intracellular Donovan bodies and vacuolated cytoplasm. Histologic section of inguinal lymph node. Hematoxylin and eosin,  $\times 1,500$ .

The only difficulty encountered was the elimination of the few contaminating bacteria. Plate cultures of bits of tissue showed that the chief contaminants were *Corynebacterium xerose* and paracolon bacilli. Because the Donovan bodies were present in far greater number than the contaminants, it was possible to isolate the former by injecting the yolks of chick embryos with a series of tissue dilutions.

In one experiment serial tenfold dilutions in sterile saline solution were made, beginning with ground granulation tissue. As all dilutions were made with the same pipet, they were crudely approximate. Of each dilution 0.1 cc. was inoculated.

1. Anderson, K., DeMonbreun, W. A., and Goodpasture, E. W. An Etiologic Consideration of *Donovania Granulomatis* Cultivated from Granuloma Inguinale (Three Cases) in Embryonic Yolk, *J. Exper. Med.* 81: 25 (Jan) 1945.

into the yolk of a five day old chick embryo. Results are presented in the table. There it may be seen that the embryos inoculated with  $10^{-3}$  and  $10^{-4}$  dilutions, respectively, died within two or three days and had diphtheroids in their yolks, whereas embryos inoculated with dilutions of  $10^{-6}$ ,  $10^{-7}$  and  $10^{-8}$ , respectively, survived to harvest and showed only Donovanias. No organisms were found in the yolk which had been inoculated with the  $10^{-5}$  dilution. Presumably the diphtheroids had been diluted out of the inoculum. On the other hand, this embryo, which had been harvested seven days after inoculation, might have shown Donovanias had it been harvested eleven days after inoculation, as were the positive embryos.

The two strains have been carried through twenty-eight and thirty passages, respectively, in embryonic yolk. The organism has shown many resemblances to those described by others. It has been a highly pleomorphic, gram-negative rod. In Wright stains it was often intensely bipolar, and "safety pin" forms were common (fig 7). Some forms were indistinguishable from the Donovan bodies seen in touch smears made directly from the ulcer on the patient. It was frequently encapsulated. Several tests for motility were negative. In harvested yolk kept at room temperature ( $20-30^{\circ}\text{C}$ ), the organisms have remained viable for four weeks, but not for ten weeks.

*Isolation of Donovanias Granulomatis*

Chick Embryo	Dilution of Tissue in Inoculum *	Fate of Chick	Time of Harvest, Days After Inoculation	Stained Smears of Yolk †
IB 7	$10^{-3}$	Died in 3 days	7	Diphtheroids
IB 8	$10^{-4}$	Died in 2 days	7	Diphtheroids
IB 9	$10^{-5}$	Alive at harvest	7	No organisms
IB 10	$10^{-6}$	Alive at harvest	11	Donovanias
IB 11	$10^{-7}$	Alive at harvest	11	Donovanias
IB 12	$10^{-8}$	Alive at harvest	11	Donovanias

\* In each case 0.1 cc of tissue dilution was inoculated into the yolk of a five day old chick embryo.

† Gram stained and Wright stained smears were examined.

Routinely, the inoculum used for passage was plated on blood agar, but the organism has never been observed to grow thereon. Blood agar, Loeffler's slants, thioglycolate broth, and infusion of beef heart containing 2 per cent horse serum failed to support growth, whether incubation was carried out in air, under 10 per cent carbon dioxide or anaerobically. On five occasions, the yolks of 2 infertile eggs have been inoculated in parallel with embryonated eggs. Regularly, the embryonated eggs supported growth, but the infertile eggs did not. In similarly arranged tests it was found that the organism was not propagated on the chorioallantoic membrane of the chick. In 6 chicks, it was found that the organisms dropped on the chorioallantoic membrane did not succeed in invading the chick and settling in the yolk, which would have offered a favorable medium for growth. Paraffin sections of the yolk stained with hematoxylin and eosin exhibited bodies morphologically similar to Donovan bodies within the yolk sac cells in 3 out of 4 embryos (fig 8).

A heat-killed "bacterial" antigen prepared from seventh passage yolk cultures was injected intracutaneously in the forearm of the patient. An area of erythema and slight induration, 12 mm in diameter, was apparent in twenty-four hours. A control site into which was injected ten times as much yolk material from uninoculated eggs showed no reaction. A subsequent test with ten times as much

antigen gave a twenty-four hour reaction that was 20 by 25 mm but not as intensely red as the preceding one

A "bacterial" antigen for complement fixation tests was prepared from infected yolk (twenty-ninth passage) by three cycles of differential centrifugation in plugged 50 cc centrifuge tubes. In the first phase of each cycle the material was spun in a size 1 International centrifuge at 3,000 revolutions per minute for one hour, and the supernatant material was discarded. The precipitate was then suspended in a volume of sterile saline solution equal to the original volume

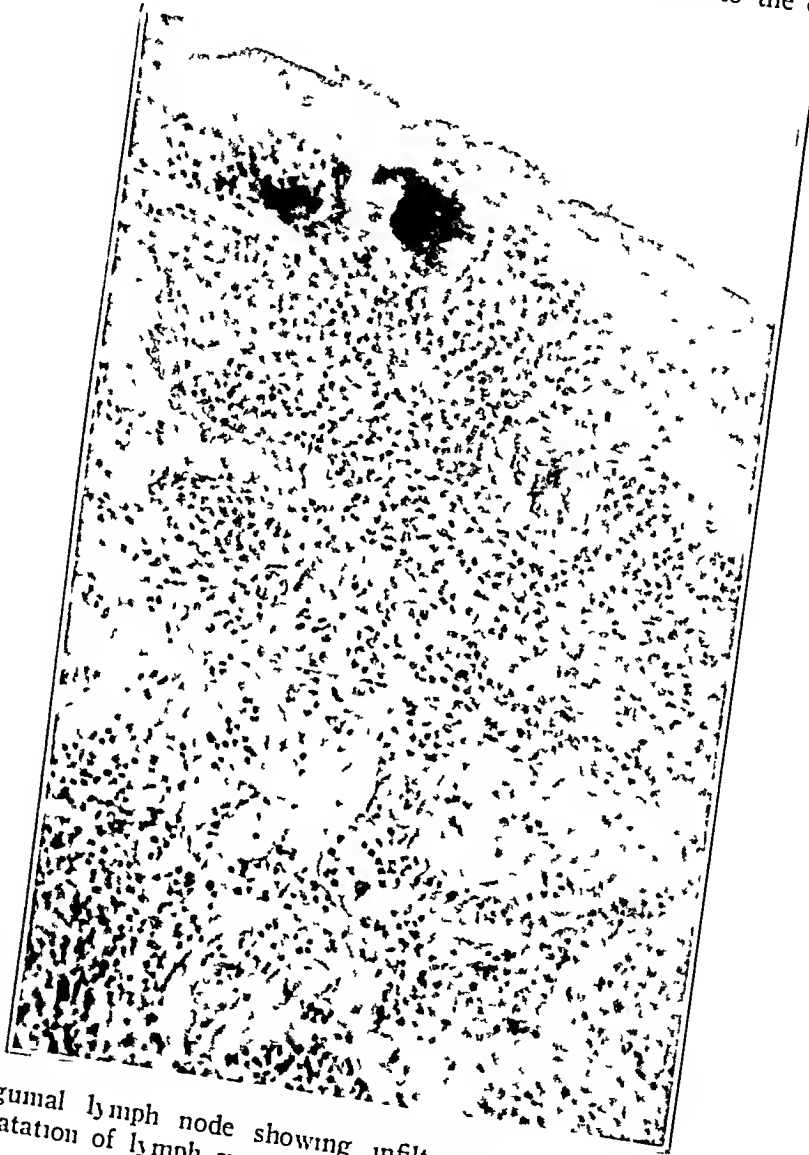


Fig 6—Inguinal lymph node showing infiltration of inflammatory cells in capsule and dilatation of lymph sinuses. Hematoxylin and eosin,  $\times 105$

of yolk. In the second phase of each cycle the resuspended precipitate was centrifuged at 600 revolutions per minute for fifteen minutes, and the sediment was discarded. The final supernatant material was diluted 1:4 and used as the antigen, without further treatment. A Gram stain confirmed the presence of the organisms. A control antigen was similarly prepared, beginning with yolk taken from un inoculated embryos of the same age as the infected ones. The control antigen was used undiluted, but was only slightly more turbid than the diluted

"bacterial" antigen Neither the "bacterial" nor the control antigen was anticomplementary

For quantitative complement fixation tests, serial twofold dilutions of serums were prepared, and 0.2 cc of serum or of serum dilution was used in each tube. Parallel tests were run with "bacterial" antigen and control antigen. Other-

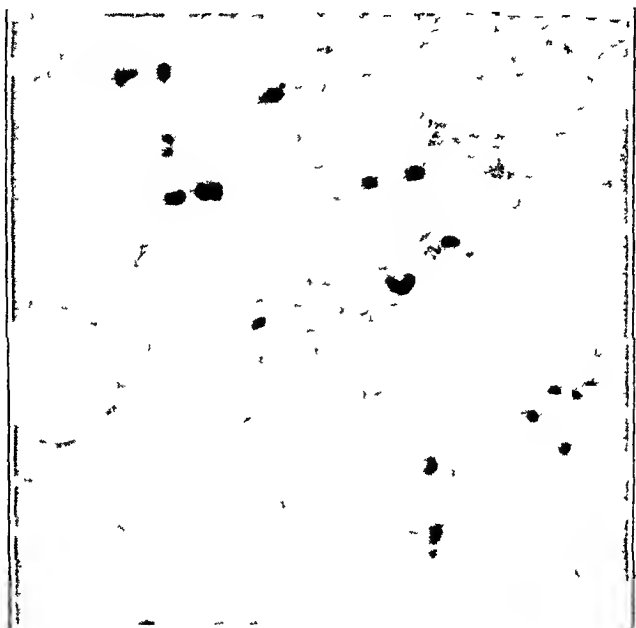


Fig 7—Smear showing Donovan bodies grown in embryonic yolk, ninth passage. Wright's stain,  $\times 1,500$

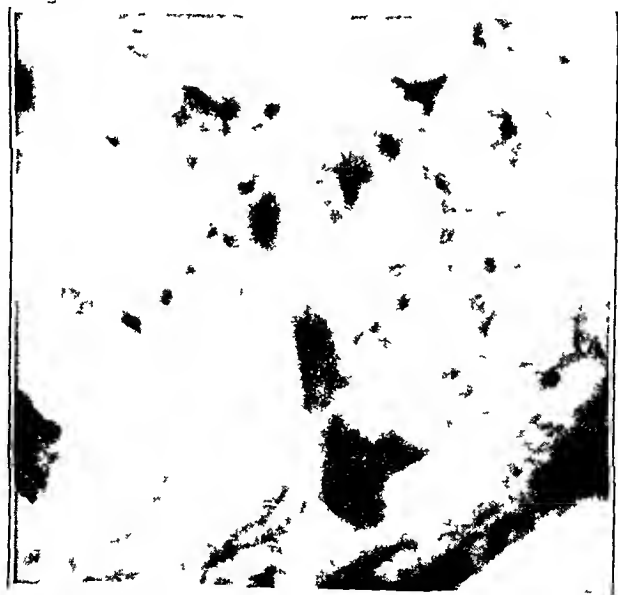


Fig 8—Histologic section of yolk sac epithelium of chick embryo with intracellular Donovan bodies, fifteenth passage. Hematoxylin and eosin,  $\times 1,800$

wise, the tests were performed as in the Kolmer simplified complement fixation test for syphilis

Serums had been collected from the patient on February 9 and April 26 and had been stored frozen. These were tested in the same run with serums from 20 normal persons which had been stored frozen. Both serums from the patient showed reactions of 4 plus in the lower dilutions, and reactions of 2 plus with an initial serum dilution of 1:64. In this series of tests nineteen of the twenty normal serums were negative, but one serum gave a reaction of 2 plus at an initial dilution of 1:2. In tests with two similar antigen preparations, weak reactions occurred with two other normal serums, however, the strongest reaction encountered with normal serum is that which has been reported. The second serum from the patient was slightly anticomplementary in the absence of antigen, and gave a plus-minus reaction with the control antigen at an initial serum dilution of 1:2. No other positive reactions with the control antigen were observed. It may be noted that ice box fixation was employed and the antigen had not been subjected to chemical treatment, two circumstances calculated to emphasize any tendency of the antigen to react with normal serums.<sup>2</sup> Nevertheless, the results clearly indicate a specific relationship between the patient's serum and the organism isolated from him.

#### COMMENT

Granuloma inguinale is a chronic disease believed to be acquired during sexual intercourse. Many authorities consider the incubation period to be twenty to sixty days. It is much more prevalent in the Negro race than the white race.

The initial lesion is a papule or vesicle the surface of which becomes eroded, leaving a granulomatous ulcer. The usual concept of the characteristic fully developed lesion is that it has a base of soft beefy red granulation tissue that bleeds easily if traumatized and has sharply defined irregular serpiginous borders that are elevated and tend to roll over on the bordering skin. There is no pain unless gross secondary infection exists.

It is interesting to note that the lesion in the present case did not initially present the typical appearance of a granulomatous lesion. Instead it was somewhat painful, and there was a considerable amount of suppuration with undermining of the skin edges and the formation of a large abscess cavity adjacent to the wall of the anus and rectum. This has been mentioned only occasionally in the literature, by Pariser and Beerman,<sup>3</sup> D'Aunoy and von Haam,<sup>4</sup> and Sobel and Pensky,<sup>5</sup> and caused delay in establishing the diagnosis in our case.

2 Wertman, K. Nonspecific Complement-Fixing Antigen in Embryonic Egg Tissues. *J Lab & Clin Med* 30:112 (Feb) 1945

3 Pariser, H., and Beerman, H. Granuloma Inguinale, *Am J M Sc.* 208:547 (Oct) 1944

4 D'Aunoy, R., and von Haam, E. Granuloma Inguinale, *Am J Trop Med* 17:747 (Sept) 1937

The definite enlargement of a lymph node in the right inguinal region, starting approximately one month after the onset of the original lesion, is of interest. It is generally accepted that granuloma inguinale is a disease of the skin and corium and not of the lymphatics. Strong<sup>6</sup> denies that the lymphatic nodes are affected, and Fox<sup>7</sup> points out that the neighboring lymphatic nodes are not enlarged. However, Greenblatt, Dienst, Pund and Torpin<sup>8</sup> were impressed by the frequency with which the inguinal lesion was preceded by a primary focus on the genitalia. In experimental production of the disease in human beings they were able to demonstrate Donovan bodies in underlying lymph nodes. They suggested that the Donovan bodies spread by way of the lymphatic system to the lymph nodes, where temporary, though mild, reactions with perilymphadenitis occur. They stated their belief that if the Donovan bodies reach the papillae and corium of the overlying skin during this process a subcutaneous granuloma is formed. Anderson, DeMonbieun and Goodpasture<sup>1</sup> aspirated material rich in Donovan bodies from two unruptured lesions in a Negro man with other ulcerative lesions of granuloma inguinale. Sobel and Pensky<sup>5</sup> reported a case in which there was bilateral inguinal adenitis, and along the lymph vessels of the dorsum of the penis two fluctuant abscesses proved to be due to the etiologic agent of granuloma inguinale.

According to Pund and Greenblatt,<sup>9</sup> there is a uniform histologic picture in pure or unmixed cases of granuloma inguinale. These authors have described the essential features consisting of (a) a massive cellular reaction in which luxuriant granulation is surcharged with plasma cells, (b) relatively few lymphocytes, (c) a diffuse sprinkling of polymorphonuclear leukocytes with focal collections in the superficies and papillae, (d) a pronounced marginal epithelial proliferation simulating early epitheliomatous changes and (e) pathognomonic large mononuclear cells within the granulation tissue. They stated their belief that the cytologic character of the large mononuclear cell together with its contained inclusion bodies permits the histologic diagnosis of granuloma inguinale to be made.

In 1939, Greenblatt, Dienst, Pund and Torpin<sup>8</sup> reported in 2 patients, 1 of whom had extragenital involvement, the presence of Donovan bodies, in the underlying cervical and inguinal lymph nodes of one and in one

5 Sobel, N, and Pensky, N. Bubonulus in Granuloma Inguinale, *Arch Dermat & Syph* **48** 494 (Nov) 1943

6 Strong, R. P. *Stutt's Diagnosis, Prevention and Treatment of Tropical Diseases*, ed 6, Philadelphia, The Blakiston Company, 1942

7 Fox, H. Granuloma Inguinale, *J A M A* **87** 1785 (Nov 27) 1926

8 Greenblatt, R. B., Dienst, R. B., Pund, E. R., and Torpin, R. Granuloma Inguinale, *J A M A* **113** 1109 (Sept) 1939

9 Pund, E. R., and Greenblatt, R. B. Specific Histology of Granuloma Inguinale, *Arch Path* **23** 224 (Feb) 1937

regional inguinal node in the other. In 1 other patient in whom the disease occurred spontaneously and in 1 patient in whom the disease was induced experimentally by inoculation of aspirated pus in the groins, the excised lymph nodes exhibited endothelial hyperplasia but no Donovan bodies. In one of the instances in which Donovan bodies were found the lymph node showed foci of suppuration. Two adjacent nodes showed only perilymphadenitis and lymphocytic infiltration of the capsule. In the present case the lymph node showed a decided but not uniform perilymphadenitis with both lymphocytes and plasma cells infiltrating the capsule. Although no definite abscesses were present in the node, the peripheral sinuses did contain a scattering of polymorphonuclear leukocytes as well as several mononuclear cells, plasma cells and lymphocytes. In addition, Donovan bodies were demonstrated in a few of the mononuclear cells. The present case, therefore, supports the concept that one of the routes of spread of granuloma inguinale is through the lymphatics. One can only speculate as to whether a lesion of the skin would have developed in the inguinal region in this patient. Unfortunately no culture studies were made of this enlarged lymph node.

It is well known that Donovan bodies do not grow on ordinary bacteriologic mediums. However, Anderson, DeMonbreun and Goodpasture<sup>1</sup> have described the cultivation of three strains in embryonic yolk. Cultivation of a fourth strain in embryonic yolk has been described by Sheldon, Thebaut, Heyman and Wall<sup>10</sup>. The Donovan organism has also been isolated and propagated by continuous tissue culture (by George O. Gey, as reported by Lyford, Scott and Johnson<sup>11</sup>). Anderson and his co-workers<sup>12</sup> have presented evidence for the etiologic relationship of their cultivated organisms to the disease granuloma inguinale, and have proposed the name "*Donovania granulomatis*" for the Donovan micro-organism, which they consider to be a bacterium with fastidious growth requirements. In its source, appearance, staining properties and biologic behavior, the present organism shows sufficient similarity to those of Anderson and his co-workers to justify its identification as *Donovania granulomatis*. Profuse growth in embryonic yolk and invasion of the yolk sac cells, as contrasted with failure to grow in the yolk of an infertile egg or on the chorioallantoic membrane have been noted by Anderson and his colleagues, who have also described skin tests with

10 Sheldon, W. H., Thebaut, B. R., Heyman, A., and Wall, M. J. Osteomyelitis Caused by Granuloma Inguinale, *Am J M Sc* **210** 237 (Aug) 1945.

11 Lyford, J., III, Scott, R. B., and Johnson, R. W., Jr. Polyarticular Arthritis and Osteomyelitis Due to Granuloma Inguinale, *Am J Syph, Gonorr & Ven Dis* **28** 588, 1944.

12 Anderson, K., Goodpasture, E. W., and DeMonbreun, W. A. Immunologic Relationship of *Donovania Granulomatis* to Granuloma Inguinale, *J Exper Med* **81** 41 (Jan) 1945. Anderson, DeMonbreun and Goodpasture<sup>1</sup>.

heat-killed "bacterial" antigen The cutaneous reactions of the present patient were qualitatively similar but less extensive

The complement-fixing antigen herein described differed from that of Anderson and his colleagues in that it was composed largely of washed organisms, whereas that of Anderson and his colleagues was mainly ether-extracted, reprecipitated "capsular substance" However, the present antigen in all likelihood contained "capsular substance" along with the organisms Although it was good enough to demonstrate a specific relationship between the patient's serum and the organism isolated from him, it would undoubtedly require modification and standardization before use as a serodiagnostic agent

The fixation of complement by the patient's serum with a lymphogranuloma venereum antigen was of dubious significance in view of the negative reactions to the Frei tests obtained for the patient and the well recognized tendency of the antigen to give reactions which are not specific for lymphogranuloma venereum<sup>13</sup>

#### SUMMARY

In a case of granuloma inguinale involving the buttock, perianal tissue and an inguinal lymph node, the onset as an acute suppurative process was atypical

The diagnosis was established by (a) the clinical appearance, (b) demonstration of Donovan bodies in the tissue and (c) response to specific treatment with fuadin

The probable etiologic organism, *Donovania granulomatis*, was cultivated in embryonic yolk The reactivity of the patient to the cultivated organism was demonstrated by positive reactions to intracutaneous and complement fixation tests

The photographs were prepared by Lieutenant Lawrence Binder

13 Florman, A L The Use of a Commercially Available Complement-Fixing Antigen for the Diagnosis of Elementary Body Types of Viral Infection, *J Immunol* **51** 29 (July) 1945

## ACNE VULGARIS TREATED WITH VITAMIN A

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**D**ISCUSSION with dermatologists results in the opinion that the majority have been unable to arrive at a conclusion as to the value of treatment of acne with vitamin A or have judged it to be of little value in spite of the rather favorable report by Straumfjord<sup>1</sup>. Published reports have been few and inconclusive. Experimental studies by Cornbleet and his associates<sup>2</sup> failed to demonstrate any lack of vitamin A in the blood of patients with acne. Obermayer and Frost<sup>3</sup> recently said that as yet they "are prepared only to state that vitamin A therapy is undoubtedly of benefit in the handling of some forms of acne vulgaris while others do not seem influenced by it."

In order to arrive at an opinion, we determined to observe the effects of vitamin A given orally in a dosage of 100,000 units daily to a group of university students with acne. About one third of the group had previously received treatment by other physicians, with little or no effect. Neither they nor those without previous treatment were given any other measure to use while taking vitamin A, and they were given no advice as to diet or hygiene. The duration, extent and severity of their acne varied within wide limits. Patients were asked to return for observation every three to four weeks.

Although 52 patients began the treatment, the reported results are based on observation of 45 patients who continued treatment for an average of four or five months, a period long enough to allow formation of an opinion of the value of the treatment. The majority of the patients were women. In 46 per cent of the cases results could be classed as good, though in only 1 case could the acne be spoken of as cured. Twenty-seven per cent of the patients had slight improvement in their

From the Student Health Service, Dr. Ruth Boynton, Director, and the Division of Dermatology, Dr. H. E. Michelson, Director, University of Minnesota.

1. Straumfjord, T. V. Vitamin A. Its Effect on Acne, *Northwest Med* 42: 219 (Aug.) 1943.

2. Cornbleet, T., Popper, H. and Steigmann, F. Blood Vitamin A and Cutaneous Diseases, *Arch. Dermat. & Syph.* 49: 103 (Feb.) 1944.

3. Obermayer, M. E. and Frost, K. Some Phases of Vitamin Therapy in Dermatology. *Arch. Dermat. & Syph.* 51: 309 (May) 1935.

eruptions, and 27 per cent showed no improvement (Although there was apparent variation based on sexual difference, the series was small and statistical analysis indicated that the difference was probably not significant)

While no untreated patients were simultaneously observed in order to control the conditions of the experiment, two previously recorded series of comparable material are available for analysis. During a period of observation changes classed as "good" were noted in 55 per cent of a group given nicotinic acid,<sup>4</sup> in 41 per cent treated topically with an estrogenic cream and in 43 per cent using the same cream but without estrogenic content.<sup>5</sup> In comparison with these figures it is apparent that vitamin A does not produce remarkable improvement in acne. In comparison of these results with those reported by Straumfjord, it is noted that he was able to review the results in only 20 per cent of his original group of 300 cases. While 79 per cent were ultimately free or nearly free from the eruption, the improvement usually occurred after three months of treatment and often did not occur until after nine

*Results of Treatment with Vitamin A*

	Unimproved	Slightly Better	Good	Total
Females	8	8	18	34
Males	4	4	3	11
Total	12	12	21	45
	27 per cent	27 per cent	46 per cent	

months. In our experience it was usually difficult to persuade the patient to continue oral therapy without other measures when considerable improvement failed to result after six or eight weeks of treatment.

The real value of treatment cannot always be judged by the per cent of persons showing improvement. In this series of patients there were 5 persons who had satisfactory improvement while taking vitamin A but whose eruption became worse after the treatment was stopped, only to improve again when treatment was reinstituted. Are such results the effect of psychotherapy? Such a conclusion seems unjustified since the treatment was offered to these patients without extravagant claims for recognized value. The case of Saunders<sup>6</sup> seems not to be explicable as a result of psychic influence.

4 Lynch, F W. Nicotinic Acid in the Treatment of Acne Vulgaris, Arch Dermat & Syph **42** 481-482 (Sept) 1940

5 Lynch, F W. Treatment of Acne by Local Applications of an Estrogenic Agent, Urol & Cutan Rev **45** 466 (July) 1941

6 Saunders, T S. Favorable Effects of Vitamin A in a Case of Acne of Long Duration, Arch Dermat & Syph **50** 199 (Sept) 1944

#### CONCLUSIONS

The treatment of acne by oral administration of 100,000 units of vitamin A daily seems not to be generally advantageous when continued for only three months. Probably a few persons obtain much improvement with this method of treatment.

## LEISHMANIASIS VERRUCOSA OF THE FACE

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**L**EISHMANIASIS verrucosa must be studied with special attention because it closely resembles many other verrucous manifestations, such as verrucous syphilides, verrucous tuberculosis and verrucous leproma. The size of the plaque in verrucosa leishmaniasis varies greatly, its outlines are well defined, and it is situated on healthy or slightly erythematous (but never edematous) skin.

The lesion itself is raised and whitish gray and consists in furrows arranged in squares which bound nipple-like projections of uniform height, so that the lesion presents a uniform surface.

According to Canal Feijoo,<sup>1</sup> on inspection one has the impression of looking at a thick crust which completely covers some lesion on which the crust was formed. But when an attempt is made to remove the crust one finds that it is a proliferative lesion. The grooves which divide the nipples are 4 to 5 mm deep. These nipples are formed of firm tissue, but Canal Feijoo<sup>1</sup> declared that they change their shape under the action of traction or pressure, however, when this traction or pressure ceases, the nipples do not recover their original form. The color of the lesion varies at different levels, it is whitish gray on the surface and pale rose, almost white in its deeper part.

The lesion begins and ends on healthy skin and therefore is not localized on an infiltrated base. It is not exudative but completely dry. Its site of election is the lower limbs. It must be stated, however, that Canal Feijoo<sup>1</sup> (and he alone) saw this lesion in the cervical part of the cephalic region, on the same site where keloidal acne is found. Rabello<sup>2</sup> affirmed that verrucous and frambesical lesions are more commonly met with on the lower limbs. Large verrucous plaques may occur, with, at times, points of regression side by side with spots where the disease is progressing.

My case is worthy of note because of the extremely rare localization of verrucosa leishmaniasis of the face.

1 Canal Feijoo, E. J. Particularidades clinicas de la leishmaniosis cutaneo-mucosa observadas en Santiago del Estero, *Rev. med. latino-am.* **19** 953-970, 1934.

2 Rabello, E. Formes cliniques de la leishmaniose tegumentaire, in *Deuxieme congres des dermatologistes et syphiligraphes de langue française*, Strasbourg, 1923, p. 561.

REPORT OF A CASE

J P R was a Brazilian, a Negro farm worker, residing at Governador Valadares, had a family and personal history of no special interest. General examination showed nothing abnormal. Dermatologic examination showed an extensive lesion covering the back and sides of the nose, the upper lip, the inner part of the left upper eyelid and all the middle part of the left side of the face, as far as the level of the ascending ramus of the lower jaw.

The lesion consisted of a plaque, which was continuous at some points and discontinuous at others. The plaque was all warty, furrowed in various directions and whitish. The edges were well defined and the surface completely dry (fig.)



Leishmaniasis verrucosa of the face

*Laboratory Examination* - Montenegro's test elicited a positive reaction. The Kahn reaction of the blood serum was negative. Histologic examination showed leishmaniasis verrucosa.

SUMMARY

A case of leishmaniasis verrucosa is reported affecting the face which is a rare site for this disease.

RUI COSTA, 1691

# CUTANEOUS DIPHTHERIA AND TROPICAL ULCERS

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**T**ROPICAL ulcers, of diphtheritic or other origin, have been treated by a variety of methods, with varying degrees of success. With the advent of penicillin, more satisfactory results have been observed.<sup>1</sup> This report concerns itself with the bacteriologic findings and the results of several plans of penicillin therapy in 56 patients with tropical ulcers or ulcerated dermatitides. In 8 of the patients the ulcerated lesions harbored virulent *Corynebacterium diphtheriae*.

## MATERIALS AND METHODS

*Plan of Study*—The patients were admitted to special wards with isolation facilities. Schick tests were performed on admission, and the results were read on the third and fifth days, to minimize the number of falsely positive and combined reactions. Each patient was given three days of preliminary cleansing treatments, during which time material for cultures was taken daily from the nose, throat and all active lesions of the skin (ulcerations, fissures, vesicles, pustules and other lesions in which organisms might be found). The preliminary treatment consisted of the application of wet dressings of isotonic solution of sodium chloride from 8 a. m. to 4 p. m. Dressings were kept wet continuously by the application of isotonic solution of sodium chloride, oil silk was not used. To facilitate cleansing and allow access to all portions of the lesions for cultural purposes, the lesions were mechanically debrided of crusts, exudate and membranes with sterile instruments at each change of dressings. No soap, antiseptic or medicament was applied.

On completion of the three day cleansing period, each patient was placed, in rotation and without regard to clinical or bacteriologic findings or results of the Schick test, on one of four plans of treatment.

**Plan I (Controls)** Compresses of isotonic solution of sodium chloride were applied three times daily for twenty minutes, at 8 a. m., 2 p. m. and 8 p. m. After this, crusts and exudate were removed, pustules or vesicles were opened and the lesions were gently cleansed with sterile isotonic solution of sodium chloride. The surrounding skin was cleansed with 70 per cent alcohol. Dressings made of six thicknesses of fine mesh gauze bandage in 3 inch (10 cm.) lengths were soaked in isotonic solution of sodium chloride. These were firmly applied under gauze fluffs. The dressings were kept continuously wet for two hours.

From the Army Service Forces, Eighth Service Command, Harmon General Hospital, Longview, Texas

1 Liebow, A. A., and others. Tropical Ulcers and Cutaneous Diphtheria, to be published.

At the end of the two hour period the dressings were removed and the lesions air dried. Dry sterile dressings were applied each night and soaked with isotonic solution of sodium chloride before removal the following morning.

**Plan II (Penicillin Locally)** Plan II was identical with plan I except that dressings were kept wet for two hours, three times daily, with a solution of sodium penicillin in isotonic solution of sodium chloride containing 250 units per cubic centimeter.

**Plan III (Penicillin Parenterally)** Plan III was exactly the same as plan I except that, in addition, penicillin was administered intramuscularly in doses of 20,000 units every three hours for seventy-two hours (total dosage 480,000 units).

**Plan IV (Penicillin Parenterally and Locally)** Plan IV combined plans II and III, that is, penicillin was given locally as in plan II and parenterally as in plan III.

Each lesion under observation was critically evaluated at nine day intervals or earlier if there was obvious deterioration of the lesion. If healing was satisfactory, as manifested by decrease in size or depth of lesion, absence of local surrounding inflammation, lymphangitis, adenitis or development of constitutional symptoms, the treatment was considered a success and continued for another nine day period. If there was a distinct lack of improvement or if the lesion became worse (increased in size or depth, spread to new areas or caused a local reaction or constitutional symptoms) the therapy was adjudged a failure and treatment changed to the plan next in order.

The activity of all patients was restricted. Complete physical and neurologic examinations were made on admission and at frequent intervals during the period of observation. Electrocardiographic tracings were made. Pulse rates were recorded regularly and blood pressures taken twice weekly. Examination of the cerebrospinal fluid was made on most patients.

Patients were discharged from the isolation wards only after all ulcerations were completely healed, three cultures of material from the nose and throat were negative for *C. diphtheriae* and a final physical and neurologic examination revealed no abnormalities attributable to the local disease. All patients were eventually transferred to the reconditioning section or sent on convalescent furlough, from which they returned for a reevaluation. The effect of activity on the healed ulcerations could thus be evaluated.

**Laboratory Procedures**—After the first three days of preliminary cleansing and daily culturing, cultural examinations were made on alternate days throughout the period of observation. For these, Loeffler's serum agar slants, 0.2 per cent potassium tellurite-blood agar and blood agar plates were used. Isolated organisms were obtained in pure culture and identified by their fermentation reactions. The virulence of strains of *C. diphtheriae* was determined by the lethal test of a guinea pig. In more urgent cases, virulence tests were performed by the intraperitoneal injection of an emulsion of the original cultures suitably diluted. Evaluation of the bacterial flora as a whole was made on the basis of findings on the blood agar plates.

A limited number of direct examinations for other organisms were made of the tropical ulcers. These included dark field examinations for fusospirochetal organisms, sodium hydroxide preparations for fungi, Giemsa-stained scrapings for leishmania and Gram staining for a determination of the general flora. Serologic tests for syphilis were performed routinely, on Negro patients. Studies of the blood for sediment of erythrocytes were also made.

## RESULTS

*Bacteriologic Findings*—Eight virulent and thirty avirulent strains of *C diphtheriae* were isolated from 56 patients with cutaneous ulcerations. Organisms were also isolated from the fauces in 1 of the 8 patients with virulent and 14 of the 30 with avirulent organisms. Diphtheroids were isolated in 13 cases (table 1).

Of the 19 cases of tropical ulcers studied, virulent diphtheria bacilli were isolated in 3 and avirulent diphtheria bacilli in 10. Of 15 patients with ulcerations superimposed on an eczematoid dermatitis, *C diphtheriae* was found in 12, in only 2 of whom the organisms were virulent. Seven patients had ulcerated lesions superimposed on atypical lichen planus. In 5, diphtheria bacilli were found, in 1 of which the organism was virulent. In a group of 15 patients with ulcerations superimposed

TABLE 1—Incidence of *C Diphtheriae* in Ulcerations of the Skin and Its Relationship to the Schick Reaction

	Num ber of Cases	C Diphtheriae						Negative for C Diphtheriae		
		Virulent, Schick			Avirulent, Schick			Schick		
		Num ber	Nega tive	Posi tive	Num ber	Nega tive	Posi tive	Num ber	Nega tive	Posi tive
Tropical ulcer	19	3	3	0	10	6	4	6	5	1
Eczematoid dermatitis	15	2	2	0	10	7	3	3	1	2
Atypical lichen planus	7	1	1	0	4	3	1	2	2	0
Dermatitis, other	10	2	2	0	6	5	1	7	5	2
Totals	56	8	8	0	30	21	9	18	13	5

on any one of several other types of dermatitis, virulent diphtheria bacilli were found in 2 and avirulent bacilli in 6.

All patients with virulent diphtheria bacilli in the cutaneous lesions gave negative reactions to the Schick test. The incidence of positive Schick reactions was comparable in the patients harboring avirulent diphtheria bacilli and in those in whom diphtheria bacilli could not be demonstrated.

From practically every case, hemolytic *Staphylococcus aureus* was isolated. In somewhat less than 10 per cent of the cases, beta hemolytic streptococci were found. The classification of these organisms was not determined.

Motile and nonmotile forms of *Proteus vulgaris* were occasionally encountered, but in no case was this organism predominant. *Pseudomonas aeruginosa* (*Bacillus pyocyaneus*) was also occasionally isolated, in 1 case it appeared to be the predominant organism.

In none of the cases examined was there found any evidence of fusospirochetosis, localized mycotic infection, leishmaniasis, sickle cell anemia or inadequately treated syphilis.

## EVALUATION OF PENICILLIN THERAPY

*The Effect on the Bacterial Flora* Repeated cultural studies revealed that the significant pathogenic organisms (diphtheria bacilli, staphylococci and streptococci) were eliminated in an average period of four days in the patients treated with penicillin locally or penicillin parenterally and locally. In patients treated with dressings of isotonic solution of sodium chloride, either alone or together with parenteral use of penicillin, only some 25 to 30 per cent were cleared of the organisms in an average period of eight days. The value of local use of penicillin and the relative ineffectiveness of parenteral administration of penicillin in these cases are evident (table 2).

In penicillin-treated patients the gram-positive organisms were the first to disappear on culture. In stained preparations, the organisms appeared to have lost their characteristic staining qualities, and a wide

TABLE 2—*Relationship of Therapy to Bacteriologic Findings\**

Plan of Treatment	Number of Courses	Lesions with Organisms at Start of Course	Lesions Cleared During Course	Average Days	Lesions Not Cleared During Course	Efficacy, %
I Isotonic solution of sodium chloride (control)	20	8	2	8	6	25
II Penicillin locally	2	11	11	4	0	100
III Penicillin parenterally	16	10	3	8	7	30
IV Penicillin locally and parenterally	14	8	7	4	1	90

\* These data refer to diphtheria bacilli, either virulent or avirulent. Hemolytic *Staph aureus* was found in practically every case and beta hemolytic streptococci in several. These were similarly affected by the various plans of therapy. For several reasons, the role of these organisms could not be studied to an extent comparable with that of the diphtheria bacilli, but their importance in the pathogenesis and healing of the lesions must be recognized.

variation in the size of the organisms was noted. If the local application of penicillin was stopped before healing was complete, it was found that organisms could occasionally again be cultured from the lesion.

*The Effect on Healing of Ulcerations (Without Regard to Bacterial Flora)* Practically all patients treated with penicillin locally or locally and parenterally combined showed satisfactory healing of the ulcerations according to the standards previously described. With isotonic solution of sodium chloride alone some healing was observed, but the number of patients showing satisfactory progress was small (35 per cent). A higher percentage (75) per cent showed satisfactory healing following the use of dressings of isotonic solution of sodium chloride together with parenteral administration of penicillin, but the mean healing time was longer. Here again the efficacy of local use of penicillin is clear, for ulcerations which were of two to three months' duration were healed in fifteen to twenty-two days with this care (table 3).

TABLE 3—*Relationship of Therapy to Healing of Ulcerations Without Regard to Bacteriologic Findings\**

Age of Lesions and Average, Mo	Isotonic Solution of Sodium Chloride				Penicillin Locally				Penicillin Parenterally				Penicillin Locally and Parenterally			
	Un satisfactory		Satisfactory Healing		Un satisfactory		Satisfactory Healing		Un satisfactory		Satisfactory Healing		Un satisfactory		Satisfactory Healing	
	No of Cases	Heal lag	No of Cases	Mean Days	No of Cases	Heal lag	No of Cases	Mean Days	No of Cases	Heal lag	No of Cases	Mean Days	No of Cases	Heal lag	No of Cases	Mean Days
Tropical ulcers	8	7	1	11	8	0	8	18	4	1	3	32	4	0	4	18
Legionnaire dermatitis	3	2	3	12	6	1	5	12	7	2	5	14	4	0	4	16
Atypical lichen planus	2	2	0	0	4	1	3	12	2	1	1	25	2	0	2	14
Dermatitis, other	5	2	3	22	5	0	5	12	3	0	3	22	4	0	4	14
Totals	20	13	7	15	23	2	21	14	16	4	12	22	11	0	14	15
				(35%)				(91%)				(75%)				(100%)

\* These data do not include effects on the underlying dermatoses

TABLE 4—*Relationship of Therapy to Healing of Ulcerations and Clearing of Organisms\**

Number of Patients Studied	Number of Patients Treated	Isotonic Solution of Sodium Chloride (Control)				Penicillin Locally				Penicillin Parenterally				Penicillin Locally and Parenterally			
		Number of Patients Not Treated		Number of Suc cessful Courses		Number of Suc cessful Courses		Number of Failures		Number of Suc cessful Courses		Number of Failures		Number of Suc cessful Courses		Number of Failures	
		No of	of	No of	of	No of	of	No of	of	No of	of	No of	of	No of	of	No of	of
Tropical ulcers	19	16	3	8	1	7	8	8	0	4	3	1	4	4	4	0	0
Legionnaire dermatitis (ulcerated)	15	15	0	5	3†	2	6	5	1	7	3	4	4	4	3	1	1
Atypical lichen planus (ulcerated)	7	5	2	2	0	2	4	3	1	2	1	1	2	2	2	0	0
Dermatitis, other (ulcerated)	15	12	3	9	2§	3	9	5	0	3	2	1	1	1	1	0	0
Totals	56	48	8	20	6	14	23	21	2	16	9	7	11	13	1	1	1
					(30%)				(91%)						(56%)		(92%)

\* Criteria Successful indicates clearance of the organisms plus satisfactory healing, failure indicates persistence of organisms and/or poor healing, † Practically healed on admission

‡ Lesions in 1 case almost healed on admission

§ One patient had penicillin locally and parenterally shortly before coming to the study ward

*The Effect on Healing of Ulcerations Plus Effect on the Bacterial Flora* When both the healing process and the bacteriologic findings were considered, it was found that penicillin locally and penicillin locally plus parenterally resulted in the highest percentage of successful courses of treatment (91 and 92 per cent respectively). Dressings of isotonic solution of sodium chloride alone were successful in 30 per cent of the courses, when parenteral administration of penicillin was added, 56 per cent were successful (table 4).

#### THE HEALING PROCESS

In tropical ulcers treated with penicillin locally, the base assumed a clean, healthy, granular appearance within three to four days. The margins, previously rolled, tended to flatten out. Epithelization occurred from the margins and proceeded rapidly at first but later more slowly as the avascular zone became larger. The central portion was always last to epithelize and usually did so under a scab which eventually fell off.

In all cases of tropical ulcers, the scar was round or ovoid, flat or depressed, thin and atrophic, with sharply defined borders outlining the original ulcer. It was almost always more deeply pigmented than the surrounding skin. In Negroes the scar was depigmented, keloids were not observed.

In ulcerations superimposed on a dermatitis, healing left little or no scar. The underlying dermatitis, however, was not significantly affected by the penicillin therapy.

#### COMPLICATIONS

*Myocarditis* No instance of myocarditis was detected either clinically or by electrocardiogram.

*Neurologic* Two cases of peripheral polyneuritis in patients with tropical ulcers were encountered. The cerebrospinal fluid of both patients showed elevated values for the total proteins and no increase in the cellular elements. In another case a suggestive history was obtained, but there was no objective confirmation. Analysis of the cerebrospinal fluid of this person and of all other patients harboring diphtheria bacilli revealed no abnormal values. In both cases of proved peripheral polyneuritis, only avirulent diphtheria bacilli could be isolated. One patient gave a negative reaction to the Schick test. The other gave a positive reaction and so was given 20,000 units of diphtheria antitoxin intramuscularly.

*Lymphangitis* Two cases of lymphangitis were observed. In both the condition arose from infected ulcerations superimposed on eczematoid dermatitis. At the time of onset, 1 patient was being treated with

compresses of isotonic solution of sodium chloride (plan I), the other had completed a course of intramuscular use of penicillin (plan III) eight days previously. Both patients were given penicillin intramuscularly with rest and elevation of the affected extremities. Improvement was prompt and satisfactory.

*Penicillin Sensitivity*—In 4 patients contact dermatitis occurred when penicillin was applied locally, all had previously been treated with penicillin locally in the same cutaneous area. In 4 others preexisting dermatitis became hyperemic, pruritic, edematous and wet within twenty-four hours following the start of parenteral administration of penicillin. In 1 other, a generalized erythematous, maculopapular rash was noted. In 3 patients there developed delayed reactions to parenteral administration of penicillin within seven to ten days following therapy, 2 had urticarial reactions, and in 1 a serum sickness-like syndrome developed.<sup>2</sup>

*Recurrences*—There were no recurrences or breakdown of the characteristically thin scar after a thirty day period of normal activity. One patient was admitted while on convalescent furlough from another hospital for a recurrence of a tropical ulcer treated there.

#### COMMENT

In order properly to evaluate our findings, it should be pointed out that most of the ulcerated lesions were a month or more old and had been treated many times previously with a variety of antibacterial agents. This may in part account for the less frequent finding of virulent diphtheria bacilli, especially in the tropical ulcers, than reported by others.<sup>3</sup> Of 19 cases of tropical ulcer, *C. diphtheriae* were found in 13, although in only 3 were the organisms virulent. This is comparable to the incidence of virulent diphtheria bacilli found in tropical ulcers occurring in troops in overseas theaters.<sup>4</sup> There is, moreover, reason to suspect that some of the others had at one time harbored virulent organisms, because in 2 of the cases in which only avirulent organisms could be isolated a characteristic peripheral polyneuritis developed.

Virulent diphtheria bacilli were found in almost all varieties of cutaneous lesions and in the nasopharynx as well. It is generally

2 Kolodny, M. H. and Denhoff, E. Reactions in Penicillin Therapy, *J. A. M. A.* **130** 1058 (April 20) 1946.

3 Craig, C. M. A Study of the Aetiology of the "Desert," Septic or Veldt Sore Amongst European Troops and the Association with Faucial Diphtheria, *Lancet* **2** 478 1919. Cameron, J. D. S., and Muir, E. G. Cutaneous Diphtheria in Northern Palestine, *ibid.* **2** 720, 1942. Medical Circular Letter no. 14, Headquarters United States Army Forces in South Pacific Area, January 1944.

4 Livingood, C. S. Personal communication to the authors. Liebow and others.<sup>1</sup>

believed that the diphtheria bacillus is unable to penetrate the intact skin, but it is probable that once the epithelial integrity is destroyed, either by trauma or by cutaneous disease, organisms may be introduced and find a suitable medium for growth and toxin production. This is largely supported by the frequency with which trauma precedes the ulcerations from which these organisms were isolated<sup>1</sup>. The onset of the ulcerations in almost half the cases in this series followed trauma. Diphtheria bacilli would thus be fortuitous contaminants, which, once established, might produce pathologic effects in susceptible persons.

The presence of hemolytic staphylococci in almost all the ulcerations indicates some measure of secondary infection, especially in ulcerations preceded by trauma or dermatitis. This is also supported by the finding of a variety of other organisms, all rather frequent contaminants. However, staphylococci may be of greater importance, since their necrotizing power may contribute to ulceration<sup>5</sup>.

Some of the factors involved in the evaluation of the therapy are worthy of emphasis. The plans of treatment decided on were clearly prescribed. Patients were admitted in rotation without selection or regard to clinical or bacteriologic findings. Conditions were maintained constant at all times, with variation in only one factor in the successive plans. Definite standards of evaluation at stated intervals were established and rigidly followed. Two medical officers cared for all patients and consulted each other frequently, there was no change in medical personnel during the course of the study, and, finally, precisely defined nursing procedures were carried out by selected nurses. These factors permitted an objective evaluation of each of the stated plans of therapy.

The data clearly indicate that local penicillin therapy is the treatment of choice in tropical ulcers and cutaneous ulcerations superimposed on one of several types of dermatitis. As would be expected, a few patients healed satisfactorily with rest in bed, good nursing care and compresses of isotonic solution of sodium chloride. A few additional patients responded satisfactorily when penicillin was administered parenterally. Practically all, however, showed progressive healing when penicillin was used locally. Moreover, organisms disappeared more quickly, and the healing time was shortened.

No significant scarring, except in the most extensive lesions, followed the healing of ulcerations which were superimposed on a dermatitis. In the case of tropical ulcers, however, a thin, atrophic and avascular scar remained and outlined the original ulcer. In this series, none has broken down under normal activity. Nevertheless, they can be easily traumatized, and because of the large zone of avascularity healing can be difficult and slow. It is therefore important to treat

5 Unpublished data

these lesions early, while the ulcer is small, in order to prevent large avascular scars

Penicillin alone should not be expected to produce satisfactory healing. Adequate rest in bed, regular cleansing, mechanical debridement, carefully applied dressings and good nursing care were available during the period of this study and are most important adjuvants

#### SUMMARY

1 A. The bacteriologic findings in 56 patients with tropical ulcers or ulcerated dermatitides are described. From these eight virulent and thirty avirulent strains of *C. diphtheriae* were isolated. Diphtheroids were found in 13 cases.

B. Hemolytic *Staph. aureus* was isolated from practically all lesions. In slightly less than 10 per cent, hemolytic streptococci were also found. Occasional strains of *P. vulgaris* and *Ps. aeruginosa* were encountered.

2 The Schick reaction was negative in all patients from whom virulent diphtheria bacilli were isolated from cutaneous lesions. The incidence of positive Schick reactions in those with avirulent organisms was comparable to that found in patients from whom *C. diphtheriae* could not be isolated.

3 The cutaneous ulcerations were treated by one or more of four plans of therapy, which included (a) dressings of isotonic solution of sodium chloride (control), (b) local use of penicillin, (c) parenteral use of penicillin and (d) penicillin locally and parenterally.

4 An evaluation of the results showed that local use of penicillin yielded the most satisfactory results and is therefore the treatment of choice. Evaluation was made on the basis of the bacteriologic findings and the healing of the ulcerations.

5 The methods involved in this evaluation are described and discussed.

6 The importance of rest in bed, mechanical debridement, cleansing, careful dressing and good nursing care is emphasized.

# EPIDERMOLYSIS BULLOSA OF THE NEWBORN

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**T**HE CLINICAL history and the observations at necropsy of a 7 week old white girl afflicted with the rare disease epidermolysis bullosa hereditaria are presented. Herlitz<sup>1</sup> in 1935 collected 14 such cases and added 8 of his own. He defined the disease as a familial or hereditary tendency to progressive blistering of the skin and mucous membranes apparent at birth or soon after. Herlitz further stated that this type of epidermolysis differs from the classic simple and dystrophic forms in that it always leads to early death, usually occurring before the third month. Additional cases reported since 1935 are those of Davidson,<sup>2</sup> Brandberg,<sup>3</sup> Schroder and Wells<sup>4</sup> and Black, Wilhelm, Gilbert and White.<sup>5</sup> The case herein recorded is the twenty-seventh.

## REPORT OF A CASE

The patient, B. S. H., a 7 week old white girl, was admitted to the University Hospitals on Oct. 29, 1944, with the complaint of recurrent formation of numerous large blisters on the hands, feet and body. According to the mother, the pregnancy was uneventful and the child was born at about term by a normal delivery. Shortly after birth a large vesicle appeared on the upper lip and gum. The mother said that "the skin on the lip and gum seemed to pull away" as the baby's hand was removed from the mouth. The following morning large blisters containing clear fluid were seen on the thumb and about the ankles. Within the next few days vesicles and bullae, some containing clear fluid and others bloody fluid, appeared on the hands, on the wrists, over the knees and about the buttocks and vulva where the diaper rubbed. The lesions were thought by the local physician to be

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1 Herlitz, G. Congenital, Nonsyphilitic Pemphigus. A Review and Description of a New Disease (Epidermolysis Bullosa Hereditaria Letalis), *Acta pædiat* **17** 315-371, 1935.

2 Davidson, L. T. Hereditary Epidermolysis Bullosa. Report of a Case with a Résumé of the Literature, *Am J Dis Child* **59** 371-378 (Feb.) 1940.

3 Brandberg, O. A. Case of Congenital Pemphigus of Malign Type (Epidermolysis Bullosa Letalis), *Ann pædiat* **157** 162-168, 1941.

4 Schroder, C. H., and Wells, A. H. Epidermolysis Bullosa in Newborn, *Minnesota Med* **28** 128-130, 1945.

5 Black, R. A., Wilhelm, E., Gilbert, C. S., and White, C. J. Epidermolysis Bullosa in the Newborn, *J A M A* **129** 734-736 (Nov. 10) 1945.

due to "pemphigus" and were treated with sulfathiazole ointment and a yellow, perfumed, saponifiable oil containing small amounts of hydroquinoline, chlorobutanol, hydroquinone and benzoic acid. The mother stated that she had no knowledge of any eruptions of this type in her family or the father's family.

On physical examination the child was well developed and well nourished. The skin was pale with numerous vesicles and bullae, 0.5 to 3 cm in diameter, on the chest, feet, elbows, heels, vulva and buttocks. The lips were dry and fissured. There were numerous ulcerated lesions of the buccal mucosa bilaterally and on the margins of the tongue. There was one hemorrhagic bulla, 0.5 cm in diameter, on the middle of the forehead. Most of the bullous lesions contained a clear serous fluid and some a hemorrhagic fluid. The superficial layers of the skin became detached on slight friction (Nikolsky's sign). There were also areas

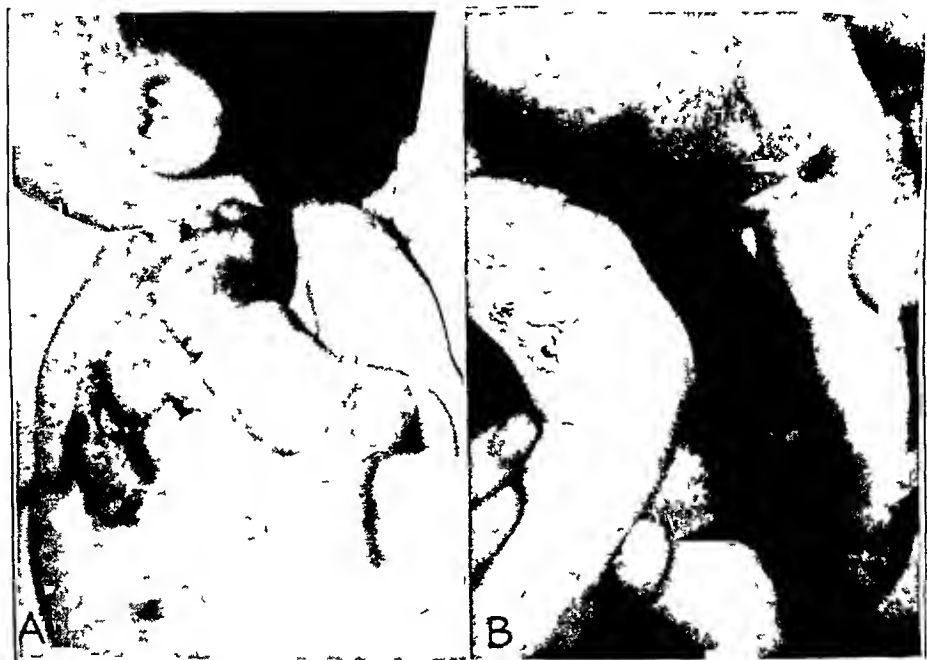


Fig 1—*A*, denuded and ulcerated areas over the skin of the chest and a large bulla over the dorsum of the left hand. *B*, denuded areas of the skin over the buttocks, thighs and right heel, with a large bulla over the external malleolus.

denuded of the superficial layers of the skin and covered by a thin serous film on the left hand and wrist, the right upper lip, the chest and both feet and ankles (fig 1). They varied from 2 to 7 cm in diameter. The nails were arched in the center and were laminated. The nail of the third finger of the right hand became detached when cleaned with a pledget of cotton, leaving an oozing bleeding surface. The nails of the third and fourth toes on the right foot were missing. Physical findings otherwise were essentially normal except for a slight enlargement of the cervical lymph nodes. The reflexes were physiologic. The temperature ranged between 99 and 101 F. The Kolmer-Wassermann reaction of the blood was negative on October 27, before the infant's admission to the hospital. The blood contained 8 Gm of hemoglobin, the red blood cell count was 2,600,000 with decided anisocytosis and some polychromasia, the white blood cell count was 10,000 per cubic millimeter, with 37 per cent neutrophils (nonfila-

mented 21 per cent and filamented 16 per cent) and 48 per cent lymphocytes, 13 per cent monocytes and 2 per cent eosinophils. The child was given multiple vitamins, crude liver extract intramuscularly and vitamin K. Moist packs of isotonic solution of sodium chloride were applied to the denuded areas and a light cradle used for heat over the body. Treatment was of no avail, and the child died at 6 30 a m on October 31.

At necropsy (sixteen hours after death) the child was well developed, well proportioned and 50 cm long and weighed 2,950 Gm. Over extensive areas on the chest, abdomen, back, external genitals, buttocks, thighs, hands and feet there was desquamation of the superficial layers of the epidermis, with crusts over some of the denuded areas. The skin elsewhere remained in folds when pinched or lifted. The scalp was covered with abundant light brown hair and was free of lesions. The anterior fontanel was sunken and measured 4 by 4 cm. The posterior fontanel was closed. The lips were crusted, and the tongue was coated. The hands, fingers, feet and toes were denuded of superficial layers of skin, and some of the nails were missing. The thymus was 2 by 2 cm and pale pink, with the lobular pattern discernible externally and on its cut surfaces. The lungs weighed 75 Gm together. The posterior portions were partly airless. Some of the bronchial branches contained aspirated material. The heart measured 3.5 cm from the base to the apex and 4 cm across the base. The chambers and their orifices were proportionate and their valves delicate. There were no anomalies of the large vessels or of the coronary sinus and its tributaries. No changes were noted in the peritoneal cavity and spleen, liver, gallbladder and biliary ducts, pancreas, esophagus, stomach and duodenum, jejunum, ileum, colon and rectum. The suprarenal glands, kidneys, urinary bladder, vagina, uterus, fallopian tubes and ovaries were normal.

Microscopic examination was made of the heart, lungs, spleen, liver, pancreas, esophagus, small and large intestines, suprarenal glands, kidneys, urinary bladder, aorta, diaphragm, thymus and skin. In the lungs in focal areas the air spaces contained a few red blood cells, some polymorphonuclear granulocytes and a pink-stained amorphous material. In the septums there were some lymphocytes, plasma cells and large mononuclear cells with occasional giant cells. The cells lining the bronchiolar and bronchial branches were well preserved. In the spleen the malpighian corpuscles were rather large, with decided overgrowth of their germinal centers. Some contained a nuclear debris free or within large mononuclear cells, and a few polymorphonuclear granulocytes. Scattered throughout the pulp there were minute blood-forming islands. In the liver there were similar blood-forming islands and some slight albuminous and fatty changes. In the tail of the pancreas some of the islands were close to one another, appearing almost confluent. There were no other changes in the acini, ducts or stroma. In the esophagus there was perfect preservation of the surface epithelium, and there were no changes noted in the tunica propria, muscularis mucosae, submucosa and muscular coats. Similarly no pertinent changes were seen in the jejunum, ileum and colon except for aggregations of eosinophilic granulocytes in the tunica propria and changes in the lymph follicles and in the mesenteric lymph nodes similar to those seen in the malpighian corpuscles of the spleen, with numerous eosinophilic granulocytes in the sinuses. In the suprarenal glands the cortical zones were narrow, with some vacuolation of the cytoplasm of the cells. The vacuolation also was seen in the medullary zone. In the kidneys the lumens of the convoluted tubules were almost obliterated by protrusion of vacuolated lining cells. In the urinary bladder the urothelium was well preserved, with the superficial layers in places loose and desquamated. In the thymus the cortical and medullary zones



FIGURE 2

(See legend on opposite page)

were proportionate. Hassall's corpuscles were fairly numerous and of good size. Some of them had a concentric debris in their centers. The connective tissue of the septums seemed spread apart. In preparations of the skin stained with hematoxylin and eosin the epidermis appeared to be separated in sheets from the corium (fig 2A). The corium was loose, fibrillar and relatively acellular, with the tissue elements decidedly spread apart. No elastic fibers were seen in preparations stained by Weigert's method. Beneath the superficial layers of the corium there were collagenous bundles, hair follicles, sebaceous glands and sweat glands, the cellular structure of which appeared intact. No change was noted in the subcutaneous adipose tissue. In preparations from the denuded area there was a delicate layer of lavender-stained material with nuclear debris on the surface. In the subjacent portions of the corium there were some infiltrations with polymorphonuclear granulocytes. The deeper layers of the corium, including hair follicles, sebaceous glands, sweat glands and the muscoli arrectores pilorum, appeared intact (fig 2B).

#### COMMENT

An infant in whom extensive bullous lesions of the skin develop at birth or soon after birth presents a diagnostic problem. However, the appearance of the lesions, localization and other circumstances are helpful in establishing a diagnosis. The bullous lesions of syphilis usually appear on the palms and soles, with no apparent relation to trauma. The vesicobullae are always turbid and usually purulent. The oral lesions of congenital syphilis may closely simulate those seen in epidermolysis bullosa, but the serologic reaction of the mother and the presence of concomitant signs and symptoms will aid in verifying them. The presence of similar lesions in other members of the family and other infants in the nursery, as well as the lack of oral lesions, will be of aid in recognizing bullous impetigo. In epidermolysis bullosa hereditaria letalis the lesions result from insignificant trauma (Nikolsky's phenomenon). They occur over the areas exposed to pressure and friction. The bullae usually contain a clear fluid, or they may be hemorrhagic. The nails are loosely attached, and oral lesions are in evidence. History of similar lesions in other members of the family in past generations is of little avail, since Herlitz<sup>1</sup> thought this fatal type of epidermolysis bullosa to be a recessive type. His 8 cases occurred in three families, 4 in one of them and 2 in each of the others. In no instance had there been a previous case in any of the families, all of whom had records to the eighteenth century.

Because the disease at present is not amenable to treatment and is fatal in a short time, early recognition is of the utmost importance.

#### EXPLANATION OF FIGURE 2

A, microscopic appearance of the margin of a denuded area toward the intact skin, with space between the elevated epidermis and corium.  $\times 152$ . B, microscopic appearance of the denuded area.  $\times 152$ .

The fundamental nature of this disease is unknown. The defect apparently is in the skin, allowing the epidermis to separate from the corium, and in the mucous membrane of the mouth. It does not involve the entodermal and mesodermal mucous membranes. The mucosae of the esophagus, intestines and urinary bladder in our case were intact. None of the changes observed at necropsy can be regarded as pertinent except those in the skin.

#### SUMMARY

The clinical history and the observations at necropsy of a 7 week old white girl with epidermolysis bullosa hereditaria are presented. The lesions consisting in focal separation of the epidermis from the corium and of the epithelium from the tunica propria of the mouth, are present at birth or appear soon after, resulting from insignificant trauma and occurring over areas exposed to pressure and friction. The observations at necropsy suggest that the only structures involved are the skin and mucous membrane of the mouth.

## BASAL CELL EPITHELIOMA IN A PSORIATIC PATCH

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**B**ECAUSE of the rarity of epitheliomatous change developing in psoriatic disease it is felt that a case recently observed is of interest to report

### REPORT OF A CASE

*History*—A white man aged 43 was first seen on Sept 29, 1945. He was admitted to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital for treatment of an eruption that involved the scalp, face, trunk, back and legs, which he first noticed at the age of 12. Since its first appearance he had not been free from it for any length of time. At the age of 21 the eruption practically covered the entire face and the trunk, and he received external palliative treatment. The patient was returned from overseas for psychiatric study. During this survey it was observed that he had psoriasis. A patch on the right side of the body, just beneath the costal cage, was suspected to have undergone malignant change. A histologic examination showed conditions compatible with basal cell epithelioma.

*Physical Examination*—The patient did not appear acutely ill and was ambulatory. He had not lost weight and did not appear ill nourished. The pupils were normal and reacted to light and in accommodation. An examination of the anterior segments of both eyeballs revealed no abnormalities. The pharynx and the teeth were normal. There was no cervical lymphadenopathy. Examination of the lungs, heart and abdomen showed nothing abnormal. The blood pressure was 130 mm systolic and 80 mm diastolic.

*Laboratory Examination*—The urine was normal. The Kahn reaction of the blood was negative. An examination of the blood revealed 100 per cent hemoglobin, 4,800,000 red cells and 7,200 white cells, with 46 per cent polymorphonuclear leukocytes, 51 per cent lymphocytes, 1 per cent eosinophils and 2 per cent mononuclear cells. The urea nitrogen content of the blood measured 18 mg, the chloride content 450 mg and the sugar content 87 mg per hundred cubic centimeters. The basal metabolic rate was + 6 per cent. Porphyrin was not present in the urine.

*Dermatologic Examination*—Involving the scalp there were many thick scaly lesions. The areas were ill defined and patchy. On the face, especially the eyebrows, on the nape of the neck and on the back, the lesions were those of typical

psoriasis covered with a micaceous scale, which could be removed. On the chest the patchy eruption chiefly involved the sternal region. These patches varied in diameter from 2 to 5 cm. On the right side of the body, beneath the costal cage, there was a large oblong lesion that clinically appeared as a psoriatic patch (fig 1). The lesion was well defined, and there was no evidence of ulceration. The border was elevated and was pearly in appearance.

*Histologic Examination*—Gross examination showed a specimen that consisted of a tiny fragment of tissue measuring 7 by 2 by 3 cm. The surface presented an irregular scaly appearance and was gray-white and firm. On microscopic examination a portion of the surface was lined by a stratified squamous epi-



Fig 1—Psoriatic patches and epitheliomatous plaque

thelium, which in turn was covered by a layer of lamellated keratin (fig 2). In several areas there were irregularly shaped masses of basal cells in the corium which were in communication with the basal layer of the epidermis. Many of the cells were spindle shaped, but the outer layer showed definite palisading. The individual cells varied in size, shape and staining characteristics. A moderate number of mitotic figures were encountered. The surrounding tissue of the corium was infiltrated by lymphocytes, plasma cells and monocytes. The appearance of the lesion was not typical of Bowen's disease.



Fig 2—Section of skin showing basal cell epithelioma

## COMMENT

The cause of malignant change in psoriasis is unknown. Hartzell<sup>1</sup> in 1899 reported 11 cases. Pozzi in 1874 and Cartaz in 1877 were believed by Hartzell to be the first to report the association of epithelioma and psoriasis. Flint and Gordon<sup>2</sup> recorded a case in which a squamous carcinoma of the scalp was associated with two rodent ulcers on the shoulder which originated in a psoriatic patch. They also mentioned a case reported by Whitfield,<sup>3</sup> in which psoriasis was associated with rodent ulcers, and a case described by Gray,<sup>4</sup> in which a rodent ulcer occurred in a patch of psoriasis in the gluteal cleft. Sequeira<sup>5</sup> stated that he had observed several cases of multiple superficial rodent ulcers that arose in patches of psoriasis. Epitheliomatous changes occurring in 3 cases of psoriasis were completely reviewed in 1933 by Wright and Friedman.<sup>6</sup> In these cases the malignant change did not occur in the diseased skin but rather on normal tissue. All these patients had psoriasis for many years, and in all of them the cutaneous epitheliomas bore a superficial resemblance to the patches of psoriasis. Charache<sup>7</sup> described a case in which the malignant transformation proved to be a squamous cell epithelioma. In our case the patient had had psoriasis for thirty-one years. He did receive local medication, but there was no history of ingestion of arsenic. A point of interest was the recurrence of the psoriatic patch over a period of years and then the final development of a basal cell epithelioma in the area. Other psoriatic lesions were present. The epithelioma was removed by surgical excision.

## SUMMARY

A case in which basal cell epithelioma developed on a psoriatic patch is described. The clinical and histologic pictures are presented.

1 Hartzell, M. B. Epithelioma as a Sequel of Psoriasis and the Probability of Its Arsenical Origin, *Am J M Sc* **118** 265, 1899.

2 Flint, E. R., and Gordon, J. A Case of Squamous Carcinoma of the Scalp, Associated with Two Rodent Ulcers on the Shoulder Originating in a Patch of Psoriasis, *Brit J Surg* **16** 321, 1928.

3 Whitfield, A. A Case of Psoriasis Associated with Rodent Ulcer, *Brit J Dermat* **18** 40, 1906.

4 Gray, A. M. H. Rodent Ulcer Occurring in a Patch of Psoriasis in the Gluteal Cleft, *Brit J Dermat* **24** 325, 1912.

5 Sequeira, J. H. *Diseases of the Skin*, ed 4, London, J. & A. Churchill, 1927, p. 558.

6 Wright, C. S., and Friedman, R. J. Psoriasis and Multiple Superficial Epithelioma, *Arch Dermat & Syph* **27** 70 (Jan) 1933.

7 Charache, H. Squamous Cell Epithelioma in Psoriatic Patches, *Arch Dermat & Syph* **38** 241 (Aug) 1938.

# TREATMENT OF MYCOTIC INFECTIONS BY INHIBITING RESPIRATION OF DERMATOPHYTES

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IT IS WELL recognized by military dermatologists that mycotic infections in soldiers constitute the most frequent dermatologic complaint Epstein,<sup>1</sup> in a recent report, stated that "the commonest dermatoses seen in the Army are those due to superficial mycotic infections" This type of cutaneous disease comprised 16.8 per cent of his cases An analysis of a group of cases by one of us<sup>2</sup> showed that superficial mycotic infections of the feet comprised 11.8 per cent of all cases in which patients reported to the dermatologic clinic It was also shown that this type of involvement was responsible for more man-days lost than any other cutaneous disease The realization of the magnitude of the problem has led the Army Air Forces to initiate an extensive study on the prophylaxis and treatment of these troublesome infections The following report comprises the results of part of that program

Previous studies in this program on the role of aeration of the feet, accomplished through the wearing of sandals in place of regular issue shoes, in the hygiene of pedal infections have been reported<sup>3</sup> The present report on a clinical study is an outgrowth of extensive laboratory investigations on the respiration and the inhibition of respiration of the dermatophytes From those laboratory studies it is believed that the criterion of inhibition of fungus respiration may serve as a useful adjunct to methods at present in use for the selection of fungicidal and fungistatic agents and for elucidation of the mechanism of action of these

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1 Epstein, E Dermatologic Practice in a Station Hospital in Southern California A Comparison with Private Practice, Arch Dermat & Syph **52** 21 (July) 1945

2 Dolce, F A Mycotic Infections of the Feet Among Soldiers, Mil Surgeon **97** 152 (Aug) 1945

3 Nickerson, W J, Irving, L, and Mehmert, H E Effect of Wearing Sandals in Reducing Foot Infections, Air Surgeons Bull **2** 120-121, 1945, Sandals, and Hygiene and Infections of the Feet, Arch Dermat & Syph **52** 365-368 (Nov-Dec) 1945

agents<sup>4</sup> In another paper,<sup>5</sup> data have been presented on the rate of oxygen consumption of four species of dermatophytes (microrespirometer determinations) together with the variation in rate for different isolates of a given species, simple methods were developed for handling fungous preparations for the respirometer to insure a minimum of damage to the mycelial organization The effect of various treatments on the rate of oxygen consumption by different species was determined The treatments included variation in  $p_{\text{H}}$ , variation in salt concentration and addition of selected inorganic compounds and various organic substances in dilute concentrations

From these experiments some working hypotheses for future investigations were framed in regard to the nature and location within the cell of enzymes controlling respiration and the classes of substances depressing respiration among the dermatophytes Among the inorganic, water-soluble salts inhibiting respiration, zinc chloride was found to be effective in dilute concentrations

TABLE 1—*Effect of Inorganic Zinc Compounds, on Oxygen Uptake by Dermatophytes*

Compound	Concentration	Organism	Change from Rate of Oxygen Consumption in Plain Buffer, %
ZnO1 <sub>2</sub>	10 <sup>-2</sup> M	E floccosum	-92
ZnCl <sub>2</sub>	10 <sup>-2</sup> M	E floccosum	-93
ZnO1 <sub>2</sub>	10 <sup>-3</sup> M	T gypsum	-24
ZnCl <sub>2</sub>	10 <sup>-4</sup> M	T gypsum	-17
ZnO1 <sub>2</sub>	10 <sup>-3</sup> M	T rubrum	-32
Zn acetate	10 <sup>-3</sup> M	T rubrum	+27
Zn(NO <sub>3</sub> ) <sub>2</sub>	10 <sup>-3</sup> M	T rubrum	-22

It was considered desirable to conduct a clinical trial with zinc chloride to learn whether or not it was of value in the control of superficial fungous infections of the skin The results of our study are not dramatically in support of zinc chloride, but we feel that the approach of using a compound of known ability to inhibit fungous respiration is of value Ideally, substances used in treatment of these fungous infections will be toxic to some metabolic process of the fungous mycelium and neutral to the tissues of the host While respiration is a convenient index of metabolic activity in mycelial organizations of these fungi, there are other indexes that might be investigated, we merely stress that the substance being investigated for toxicity to the fungi be checked for activity against metabolizing mycelial organizations (not solely against spore germination or inhibition of growth)

4 Nickerson, W J Inhibition of Fungus Respiration A Metabolic Bio-Assay Method, Science **103** 484-486 (April 19) 1946

5 Nickerson, W J, and Chadwick, J B On the Respiration of Dermatophytes, Arch Biochem **10** 81-99 (May) 1946

A group of 45 patients with superficial mycotic infections observed in the dermatologic clinic at Eglin Field, Fla., was treated with zinc chloride solution. The cases were classified clinically into three groups: acute, subacute and chronic. There were 24 acute cases, 16 subacute and 5 chronic. The treatment employed in these cases was the local application of a 1 per cent alcoholic solution of zinc chloride (1 Gm. of zinc chloride in 100 cc. of a 25 per cent aqueous solution of alcohol) on the involved areas. This was done once daily in the dermatologic clinic. The treatment was the same in the majority of the cases, regardless of the severity of the infections, organism causing the infection or location. The only departure from this procedure consisted in 10 cases in which an additional application of the solution was used by the patient before retiring and the use of a dusting powder

TABLE 2—*Clinical and Laboratory Observations in Group of 45 Cases Prior to Therapy*

Diagnosis	Cases, No.	Potassium Hydroxide Examination of Scales	Organism Isolated on Culturing
Tinea capitis	2	Spore mosaic arrangement of ectothrix	M. audouinii
Tinea pedis	26	Positive	T. gypseum (20 cases) T. rubrum (4 cases) O. albicans (2 cases)
Tinea cruris	6	Positive	E. floccosum (2 cases) T. gypseum (4 cases)
Tinea pedis et cruris	5	Positive	T. gypseum (4 cases) T. rubrum (1 case)
Tinea glabrosa	6	Positive	T. gypseum (3 cases) T. rubrum (3 cases)

consisting of equal parts of zinc oxide, tannic acid and boric acid. All the cases were grouped together in the final analysis because there was no difference in the therapeutic result. All the patients were treated on a duty status, and no effort was made to curtail their activities. Treatment was continued for an average period of twenty days. In general, treatment was continued until a cure was obtained or there was a steady progression of the infection or an acute flare-up occurred which was considered as a possible result of the treatment. The patients were thoroughly examined prior to treatment. This was done to determine beyond doubt that the cutaneous involvement was mycotic in origin and also to determine the organism responsible for the infection. Table 2 shows the results of that study.

The results of this study indicate that the fungi responsible in these cases were five in number. Two cases of tinea capitis due to infection with *Microsporum audouinii* were included. In the 2 cases the eruptions occurred in children, dependents of Army personnel. Among the soldiers the commonest fungus isolated was *Trichophyton gypseum* (in 72 per

cent of cases) *Trichophyton rubrum* was isolated in 19 per cent of the cases. *Candida albicans* and *Epidermophyton floccosum* were isolated in 5 per cent of the cases. It was also observed that *T. gypsum* was isolated in all but 4 of the cases classified as acute. In these 4 cases *T. rubrum* was isolated in 2 cases, *C. albicans* in 1 case and *E. floccosum* in 1 case.

The outcome following the use of zinc chloride solution in the group of 45 cases studied was determined. This was done from an analysis of the clinical and laboratory observations. No patient was classified as cured unless all of the following criteria were fulfilled: (1) no clinical evidence of a mycotic infection, (2) potassium hydroxide examinations of scrapings repeatedly negative for fungi and (3) repeated failure to grow fungi from the treated site.

Table 3 summarizes the results of that analysis.

TABLE 3—Results of Treatment with 1 per Cent Zinc Chloride Solution Immediately After Treatment

Diagnosis	Cases No.	Clinical Observation			Potassium Hydroxide Studies		Cultural Studies		Organisms Recovered
		Cured	Improved	Progression	Positive	Negative	Positive	Negative	
Tinea capitis	2	0	0	2	2	0	2	0	<i>M. audouinii</i>
Tinea pedis	26	4	17	5	22	4	22	4	<i>T. gypsum</i> (16 cases) <i>T. rubrum</i> (4 cases) <i>C. albicans</i> (2 cases)
Tinea cruris	6	4	1	1	1	5	2	4	<i>T. gypsum</i> (2 cases)
Tinea pedis et cruris	5	0 (pedal) 4 (crural)	3	2	4	1	3	2	<i>T. gypsum</i> (2 cases) <i>T. rubrum</i> (1 case)
Tinea glabrosa	6	3	3	0	3	3	3	3	<i>T. rubrum</i> (2 cases) <i>T. gypsum</i> (1 case)

Eleven patients fulfilled the requirements immediately after the treatment set up for a cure in this study. However, of this group, there were 5 patients in whom the infection recurred after a ten day observation period. The 5 cases were classified as recurrences because the same organism was isolated as on the original investigation and the same site was involved. This reduces the number of cured patients to 6, or 13 per cent. Four cases of recurrence occurred in the group of pedal infections. Thus there were no patients with pedal infections cured. It was evident from a careful analysis and observation of the cases that the use of zinc chloride solution had little or no effect on pedal infections. The improvement noted in the 17 cases of pedal infection was so slight that it would be difficult to ascribe it solely to the use of zinc chloride solution. All the soldiers under treatment were impressed with the proper hygiene of their feet, the necessity of keeping their feet dry and the methods of reducing hyperhidrosis. The improvement noted could well have been due to their improved hygiene of the

feet Some of the soldiers stated that there was a decided decrease in the itching after the first few applications of the zinc chloride solution However, their relief was not of a permanent nature, because soon, with continued treatment, all volunteered that the itching returned in the same degree and annoyance as before

In the group of crural infections there were 4 patients, or 66 per cent, that fulfilled the requirements for cure immediately after treatment There was 1 patient with a recurrent eruption among these 4 cured patients after an observation period of fifteen days It was noted that the crural infections responded to this form of treatment more favorably than the pedal infections This was more forcibly brought out in the group of 5 cases in which both crural and pedal infections occurred Here the crural infections cleared up or were definitely improved, while the pedal infection was unaffected There were 6 patients with infections of the smooth skin, 3 were classified as cured and 3 as improved

It was not possible to draw any definite conclusion from this small group of cases, because of the short period of observation A comparison with a similar group of patients, treated by the usually advocated methods showed that the results with zinc chloride solution as employed by us in this study were inferior for pedal infections and approximately equal for crural infections

The cases were grouped in accordance to the organism isolated and the results obtained This was done to determine whether there was some difference in response to zinc chloride solution therapy depending on the causative organism

As a result of the grouping given in table 4, there appeared to be a difference in response depending on the infecting organism There

TABLE 4—*Organisms Isolated and Results Obtained*

Organism	Cases, No	Patients Cured	
		Number	Per Cent
<i>M. audouinii</i>	2	0	
<i>T. gypsum</i>	31	3	9.6
<i>T. rubrum</i>	8	1	12.5
<i>E. floccosum</i>	2	2	100
<i>C. albicans</i>	2	0	

was no response to treatment in the infections caused by *M. audouinii* and *C. albicans*, whereas the 2 patients with eruptions caused by *E. floccosum* were cured

A number of complications were observed during the course of zinc chloride therapy

Lymphangitis	3 cases	} 29.1 per cent of acute cases
Id eruption on fingers and trunk	2 cases	
Cellulitis	2 cases	

All these complications occurred in the cases classified as acute. Four of the patients required hospitalization after the onset of these complications. It was felt that in some way the use of zinc chloride solution in the acute cases aided the occurrence of these complications. Some of the soldiers complained of smarting, burning and pain following the use of the solution. This was especially so when the solution was applied on a denuded area. In 2 cases not included in this group, the complaints were so great that the zinc chloride was stopped after a few applications. In 3 cases the application of zinc chloride was followed each time by edema and erythema over the involved area. This was transitory and subsided in a few hours.

A number of patients (in addition to those in the group of 45 cases) were treated with a solution of zinc chloride to which had been added 0.25 per cent phenol and 2 per cent salicylic acid. This combination suggested itself following the laboratory investigation in which the addition of phenol and salicylic acid enhanced the *in vitro* respiratory-inhibitory effect of the zinc chloride on fungi. Although the number of cases in which this combination was tried was too small to draw any conclusions, it seemed a more promising preparation and one which should be given further clinical trial for both pedal and crural infections. This compound was used in cases of *tinea glabrosa* and in only a few cases of *tinea pedis*. It was much more effective in the former type of case.

#### SUMMARY AND CONCLUSIONS

1 A group of 45 patients with superficial mycotic infections observed on an Army post were treated with a 1 per cent alcoholic solution of zinc chloride.

2 Zinc chloride solution, as employed by us in this study, in spite of its action as an inhibitor of fungous respiration in a laboratory investigation, has proved to be inferior to other methods of treatment for pedal infections. Its use in crural dermatoses and in *tinea glabrosa* seems worth further study.

3 Our purpose in this report has been not to add a new chemical to the already endless list used in the treatment of these troublesome infections but to present a new method of approach, with the hope that this might stimulate further investigation along these lines.

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## REACTIONS IN THE TREATMENT OF SYPHILIS WITH PENICILLIN

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**G**REAT strides have been made in the treatment of early syphilis with penicillin, and reports seem to bear out the belief that penicillin will be an important factor in the management of syphilis. Because of the dominant position assumed by penicillin in the treatment of syphilis, it is important to consider the reactions that may be encountered in the course of therapy. It has been found convenient to classify these reactions in two groups. The first group of reactions is caused directly by penicillin, and the second group of reactions is due indirectly to penicillin and consists in reactions to the products of destruction of the spirochetes.

On review of the literature in the consideration of the first group of reactions, that is, those due directly to penicillin, it is noted that although penicillin has been accepted as the most effective and least toxic chemotherapeutic agent, widespread use of this potent antibiotic in various fields of treatment since its introduction has, however, brought forth manifold reports of reaction. According to Keefer,<sup>1</sup> in 2 to 5 per cent of all patients treated with penicillin urticaria developed. The urticaria is usually mild and disappears in spite of the continuance of treatment. In some instances, the urticaria is severe and extensive. Flinn and associates<sup>2</sup> observed cases of severe urticaria from one lot of penicillin. Intradermal tests with this brand and with two others caused positive reactions. Cutaneous tests with a fourth brand elicited negative reactions, however, and administration of this penicillin gave no reaction. Reactions from local application of penicillin were described by Michie and Bailhe.<sup>3</sup> The development of bullous dermatitis (dermatitis medicamentosa) was described by Morris and Downing<sup>4</sup> in a patient who had received 1,000,000 units of penicillin for a postoperative infection. In this patient there developed erythema and edema of the

From the Venereal Disease Division of the United States Marine Hospital

1 Keefer, C S. *Am J M Sc* **210**:147 (Aug) 1945

2 Flinn, L B, McGee, L C, Featherstone, W P, and Kern, D O. *Delaware M J* **17**:133 (July) 1945

3 Michie, W, and Bailhe, H W C. *Brit M J* **1**:554 (April 21) 1945

4 Morris, G E, and Downing, J G. Bullous Dermatitis (Dermatitis Medicamentosa) from Penicillin, *J A M A* **127**:711 (March 24) 1945

left hand, arm and left side of the body four days after the last injection of penicillin. Tense pitting edema of the entire hand and forearm was present two days after the onset of the reaction. This case showed great similarity to 2 cases which will be described further in the course of this paper. Barker<sup>5</sup> described 2 cases of sensitivity of the skin to penicillin. The first case was that of a medical officer who noted during course of contact with the drug edema of the lids and a vesicular eruption. The second case was that of a soldier in whom, after receiving injections of penicillin for five days, there developed giant urticaria, which persisted for four weeks. Both patients demonstrated positive cutaneous reactions with penicillin.

The Herxheimer reaction has been stated by Stokes to occur synchronously with the hours of greatest destruction of spirochetes by an antisyphilitic drug. This reaction has been postulated to be due either to an irritative reaction to increased liberation of toxins by still living spirochetes or to the protein-decomposition products and endotoxins resulting from their destruction. A review of the literature reveals that this reaction, due indirectly to the action of penicillin and comprising the second group of reactions heretofore mentioned, has been noted by many investigators in the field of penicillin antisyphilitic therapy. Mahoney and colleagues,<sup>6</sup> in one of the first reports on the treatment of early syphilis with penicillin, noted symptoms suggestive of a Herxheimer reaction. More and more reports have come out since then describing this group of symptoms, and they have finally been accepted as a true Herxheimer reaction. Leifer and Martin,<sup>7</sup> in a recent report, stated that 85 per cent of their patients with early syphilis demonstrated a Herxheimer reaction.

In the course of treating approximately 70 patients per month with penicillin for syphilis, the opportunity has been presented to observe numerous and varied reactions. As previously mentioned, these reactions were divided into two groups: (1) those due directly to penicillin and (2) those due indirectly to penicillin (Herxheimer reaction). The first group was further subdivided into three divisions: (a) pruritic, (b) dermatophytid and (c) post-treatment.

#### REACTIONS DUE DIRECTLY TO PENICILLIN

*Pruritic Reactions*—Pruritic symptoms were observed during the first few days of treatment and were similar to those described by Keefer. The patients usually complained of mild generalized pruritus.

5 Barker, A. N. *Lancet* **1** 17 (Feb 10) 1945.

6 Mahoney, J. F., Arnold, R. C., and Harris, A. *Penicillin Treatment of Early Syphilis*, *Am J Pub Health* **33** 1387 (Dec) 1943.

7 Leifer, W., and Martin, S. P. *Effect of Penicillin on Course of Early Syphilis*, *J A M A* **130** 202 (Jan 26) 1946.

and dryness of the skin, and in some a fleeting erythematous eruption was noted. Continued administration of penicillin in this group did not aggravate the symptoms, but instead the symptoms disappeared.

*Dermatophytid Reactions* Reactions directly attributable to penicillin therapy were noted in patients who had fungous infections. In some instances the patients stated that they had been completely free from symptoms of fungous infection at the time the penicillin treatment was begun and that they had suffered symptoms of a dermatophytid reaction after receiving penicillin for a few days.

In the cases in which the infection was already present there was an exacerbation of symptoms. Patients usually complained of a flare-up of the eruption associated with severe pruritus and clinically exhibited the classic picture of a dermatophytid reaction. These findings were explained on the bases of an allergic reaction to a common antigen. The id reaction in these cases is probably due to a common antigen present in the penicillin administered. In a typical case illustrating this type of reaction, the following facts were noted:

On Feb 17, 1946, three days after commencement of administration of penicillin, the patient (J R) noted severe pruritus of the dorsum of the fingers, web spaces and between the toes. He stated that these symptoms were similar to and severer than those experienced during the previous period of fungous infection. The patient gave a history of having had "athlete's foot," which had been absent for some time prior to admission. The lesions exhibited were vesicular in character and present in the areas of pruritus. There was some excoriation between the fingers and toes. The eruption cleared two days after the cessation of penicillin therapy without medication.

*Post-Treatment Reaction* The third group of symptoms directly due to penicillin was noted in patients who had already completed treatment. The following 4 cases illustrate some types of post-treatment reactions to penicillin encountered. It is the experience in this unit that approximately 5 per cent of the patients receiving a full course (one week) of penicillin therapy will show some form of post-treatment reaction, usually a cutaneous one.

J B was admitted on the day following conclusion of treatment for primary syphilis. He had received a full week's treatment with penicillin, a total of 1,700,000 units. The patient noted urticaria about twelve hours after conclusion of treatment. On awakening on the day following his departure from the hospital, he noted that his face, forearms, feet and legs were swollen. Associated with this severe swelling he experienced itching over his entire body. He gave no previous allergic history. Physical examination revealed a 45 year old white man who was well built and whose hands, forearms, feet, legs and face were swollen. His eyes were mere slits because of the swelling of his eyelids. There was a pretibial pitting edema (4 plus). The areas swollen were erythematous. There were large urticarial wheals over the thighs and trunk. In the few areas which were moderately clear he exhibited decided dermatographia. On the dorsum

of both wrists there were large bullae filled with clear fluid. The conjunctivas were injected.

*Clinical Course*—The patient was made comfortable with local applications of calamine lotion with 1 per cent phenol and 10 per cent calcium gluconate intravenously. At one point epinephrine was given, without much benefit. The bullae on the wrists broke on the third day of hospitalization, and the edema had completely disappeared by the fourth day. The patient was discharged on the sixth day, with the skin clear except for the denuded areas underlying ruptured bullae. A cutaneous test was made with penicillin and the patient exhibited a pronounced urticarial reaction at the site of the injection.

The patient (P. W.) was admitted complaining of swelling of hands, feet and face, associated with severe pruritus. The patient had received treatment for latent syphilis and was given a total of 3,400,000 units of penicillin over a period of one week. On the fifth post-treatment day he noted gradual swelling of his hands and feet and a severe itching of these regions. The symptoms were slow in onset. The patient gave no previous allergic history. Physical examination revealed a well built, well nourished, light-complected, white, 25 year old man who appeared to be in severe discomfort. The feet were swollen, and pretibial edema (3 plus) was noted. His face and hands were similarly edematous, and most of the regions named exhibited erythema. Giant urticarial wheals were present over the abdomen, back and thighs. The patient complained of severe pruritus, and scratch marks were noted over many portions of his body. As the patient stated, he looked like "a swollen boiled lobster." His temperature was 100 F.

*Clinical Course*—During the first and second days the temperature was elevated to as high as 102 F. He was given rest in bed, bland diet and calamine lotion with 1 per cent phenol to control the pruritus. He also received calcium gluconate intravenously and barbiturates orally. He showed improvement and was discharged after four days of hospitalization. The edema subsided on the third day of hospitalization.

A patient (W. S.) was treated for latent syphilis over a period of one week and noted the onset of urticarial wheals over the lower part of the abdomen and back twelve hours after the completion of penicillin treatment. There was severe pruritus associated with the wheals. The condition resolved itself one day after onset. A cutaneous test on the forearm with penicillin in this case produced large urticarial wheals on the forearm.

A patient (V. S.) received 3,400,000 units of penicillin over a one week period of treatment and noted a macular eruption over his arms, back and neck twenty-four hours after the therapy was completed. The reaction disappeared after being present for one day. There was a moderate amount of itching associated with this eruption. The cutaneous test with penicillin in this case also elicited a positive reaction.

#### REACTION DUE INDIRECTLY TO PENICILLIN (HERXHEIMER REACTION)

The second group in this classification—and in our mind the most important group of reactions noted—was classified as a Herxheimer reaction. The Herxheimer reaction was observed in approximately 90 per cent of the patients with early syphilis treated. The characteristics of the Herxheimer reaction noted in the order of their frequency were fever, chills, edema and pain at the site of the lesion, nausea, general malaise, headache and pains in the joints. Although the Herx-

heimer reaction is not a penicillin reaction per se, since it is felt by many to be a reaction to the products of destruction of the spirochetes, it has been emphasized in this paper because it is a fairly constant finding in patients with early syphilis treated with penicillin.<sup>8</sup> In a typical case, the patient usually notices fever from two to eight hours after the beginning of treatment. The fever is soon followed by chills and pain at the site of the primary lesion. These symptoms and the other symptoms noted previously usually persist from twelve to twenty-four hours after the beginning of treatment. In cases of secondary syphilis, arthralgia and general malaise are more commonly encountered than in primary syphilis. A fairly constant finding in secondary syphilis is the flare-up of eruptions after penicillin therapy has been begun. Frequently in cases of primary syphilis in which careful examination of the skin previously revealed no eruption present eruptions of secondary syphilis appeared after the commencement of penicillin therapy, sometimes to fade within four to twelve hours.

#### COMMENT

The reactions encountered in the course of treatment of syphilis with penicillin can be classified into two groups. In the first group are included the reactions due directly to penicillin. In this classification are included the symptoms which appear shortly after treatment has been begun and pass away in spite of the continuance of penicillin administration. This reaction group may be termed the "early treatment pruritic reaction group." Only approximately 5 per cent of the patients treated exhibited this form of reaction. The "dermatophytid reaction group" provides the second category of reactions noted. It is suggested that the active principle responsible for this reaction is an antigen present in penicillin. This reaction has been noted in the administration of various brands of penicillin. It is my impression that a common antigen exists in both the penicillin and the fungus responsible for the past or present infections. The most serious types of reactions were encountered in the "post-treatment reaction group." The symptoms were varied as to type, time of onset, severity and duration. In some, the severity of the reaction necessitated hospitalization. In the more serious conditions, serum sickness accompanied severe reactions of the skin. This group is similar to reactions noted in other papers and probably is due to sensitization developed over a long period of administration of penicillin.

The Herxheimer reaction in early syphilis treated with penicillin comprises the second group of reactions noted, or reactions due indi-

<sup>8</sup> Fromer, S., Cutler, J., and Levitan, S. Masking of Early Syphilis by Penicillin Therapy in Gonorrhea, *J. Ven. Dis. Inform.* **27**: 7 (July) 1946.

irectly to penicillin. The findings, namely, fever, chills, edema and pain at the site of the chancre are fairly typical. This reaction, because of its frequency in early syphilis treated with penicillin, should be added to the other findings, viz., history of exposure, symptoms presented, clinical picture and positive results on dark field examination, which are usually recorded in a well rounded picture of a case. Its addition provides further significant evidence in the complete, final diagnosis of early syphilis.

In no case in which reactions directly attributable to penicillin were noted could any one brand of penicillin be incriminated, because in the course of treating any one patient many brands were used.

#### SUMMARY

1. Review of the literature reveals that more and more types of reactions to penicillin are being noted during and after penicillin therapy.

2. Observations in the treatment of syphilis with penicillin revealed that there were four types of reactions encountered. These reactions were divided into two groups and three subdivisions. I, reactions due directly to penicillin ([a] early treatment pruritic [b] dermatophytid and [c] post-treatment) and II, reactions due indirectly to penicillin ([a] Herxheimer reaction).

Dr. John C. Cutler tendered many helpful suggestions in the preparation of this paper.

# UNDECYLENIC AND PROPIONIC ACIDS IN THE PREVENTION AND TREATMENT OF DERMATOPHYTOSIS

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AND

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**T**HIS article summarizes the results of three large series of experiments performed under the direction of the Research Division of the Bureau of Medicine and Surgery of the United States Navy. The object of the experiments was to ascertain as accurately as possible the efficacy of certain fatty acids and their salts in the prophylaxis and treatment of dermatophytosis<sup>1</sup>

The first and third studies were made at the United States Naval Disciplinary Barracks, Hart's Island, New York, during the later part of the summer of 1944 and throughout the summer of 1945. In these two experiments a comparatively small number of men were studied under the particularly favorable experimental conditions, arising from the fact that the subjects were all prisoners and could be kept under close and constant observation and control. These men were studied by the Hart's Island paired comparison method. This method consists in the application of two different agents simultaneously to bilateral, symmetrically situated areas of skin and the evaluation of their relative efficacy. As used here, one remedy was applied to one foot and a second to the other foot of the same volunteer. The technic and advantages of the procedure have already been described<sup>2</sup>

The second series of studies was carried out in three different Naval establishments, all situated in Florida, in locations where semitropical

The opinions or assertions contained herein are the private ones of the authors and are not to be construed as official or reflecting the views of the Navy Department or the Naval Service at large

1 In this report the terms "dermatophytosis" and "fungous infection" should not be taken literally. They are employed here to designate the signs and symptoms commonly attributed to fungous infection of the feet

2 Shaw, H. C. Comparative Evaluation of Preparations for the Prophylaxis and Treatment of Fungous Infections of the Feet and Groins by Means of Screening Tests in Human Volunteers, Report of Research Project X-448, Bureau of Medicine and Surgery, 1945. Sulzberger, M. B., and Kanof, A. Comparative Evaluation of Preparations for the Prophylaxis and Treatment of Fungous Infections of the Feet, Report of Research Project X-448, Report No. 2, Bureau of Medicine and Surgery, 1945

3 Sulzberger, M. B., Shaw, H. C., and Kanof, A. Evaluation of Measures for Use Against Common Fungous Infections of Skin, U. S. Nav. M. Bull. 45: 237-248 (Aug.) 1945

climatic conditions were approximated<sup>4</sup> In these studies different groups of men used one agent on both feet The incidence of infection for each medicament was recorded for each different group instead of comparing the efficacy of two agents by applying one to each foot of the same person

The details of the conditions under which the experiments were carried out, of the experimental procedures and of the results obtained are given in references<sup>5</sup>

The formulas of the fatty acid preparations studied were as follows

	Per Cent
Undecylenic acid-undecylenate powder <sup>6</sup> (pigmented)	
Zinc undecylenate <sup>6</sup>	20 0
Purified talc, U S P	76 0
Undecylenic acid, grade AA	2 0
Dibenzo thio indigo (red)	2 0
Sodium propionate powder <sup>6</sup> (pigmented)	
Sodium propionate (Mycoban)	20 0
Purified talc, U S P	79 5
Polychloro copper phthalocyanine (green)	0 5
Sopronol powder <sup>7</sup> (pigmented)	
Calcium propionate	15 0
Zinc propionate	5 0
Purified talc, U S P	79 5
Polychloro copper phthalocyanine (green)	0 5
Undecylenic acid-undecylenate ointment <sup>6</sup> (pigmented)	
Undecylenic acid, grade AA	5 0
Triethanolamine	3 0
Zinc undecylenate <sup>6</sup>	18 0
propylene glycol, N F	10 0
Carbowax 1500	19 0
Carbowax 4000	29 6
Distilled water	15 0
Dibenzo thio indigo (red)	0 4

In addition, the following powders were included in these studies

	Per Cent
Boric acid-salicylic acid powder <sup>8</sup> (pigmented)	
Salicylic acid, U S P (powder)	2 0
Boric acid, U S P (impalpable powder)	6 0
Zinc stearate, U S P	3 0
Purified talc, U S P	86 5
Dibenzo thio indigo (red)	2 0
Polychloro phthalocyanine (green)	0 5
Diodoquin (powder) <sup>9</sup>	
Diodoquin	5 0
Purified talc, U S P	95 0
Vioform (powder) <sup>9</sup>	
(a) Vioform (powder) 1 0    (b) Vioform (powder)	3 0
Purified talc, U S P 99 0    Purified talc, U S P	97 0
Talcum powder	
Purified talc, U S P	100 0
Foot powder, U S N, contract #N140S 14632A	
Sodium bicarbonate U S P	10 0
Sodium borate, U S P	5 0
Kaolin, N F	35 0
Purified talc U S P	38 0
Sodium perborate, U S P	10 0
Titanium dioxide	1 0
Chlorthymol N F	0 5
Methyl salicylate, U S P	0 5
Thiourea (powder)	
Thiourea	5 0
Purified talc U S P	95 0

4 Shaw, H C Comparative Evaluation of Preparations for the Prophylaxis and Treatment of Fungous Infections of the Feet and Groins II Report of Studies Made Under Field Conditions in a Subtropical Climate, Report of Research Project X-448A, Bureau of Medicine and Surgery, 1945

5 Footnotes 2, 3 and 4

6 Supplied by Wallace & Tiernan Products, Inc, Belleville, N J

7 Supplied by Mycoloid Laboratories, Inc, Little Falls, N J

8 Supplied by G D Searle & Co, Chicago

9 Supplied by Ciba Pharmaceutical Products, Inc, Summit, N J

## INCIDENCE OF DERMATOPHYTOSIS

For the purpose of recording the natural incidence of infection, only experiments II and III are summarized here. Experiment I is omitted because it included only a few men. In experiments II and III relatively large numbers of men were studied, and the two experiments were conducted during approximately the same period. Results were as follows.

*A Unselected Men* (men in whom infections were found at the beginning of the experiment, in the course of routine examinations conducted to select subjects for the prophylactic studies)

	Men Examined	Incidence of Infection, %
Florida (March to August 1945)	4,720	23.8
New York (May to July 1945)	1,152	14.0
Total	5,872	21.9

*B Selected Men* (men having uninfected feet at the first examination and used as "controls") These figures show the incidence of foot infection while under observation and without treatment or prophylactic measures.

	Feet Examined	Incidence of Infection, %
Florida (March to August 1945)	2,768	28.0
New York (May to July 1945)	531	30.9

(In the men from Florida both feet were untreated during the experiment. In the men from New York, one foot was powdered daily with one of the agents and the other foot was the untreated control included here.)

The statistics confirm the fact that dermatophytosis is a widespread disease. The greater initial incidence in Florida over that in New York was to be expected. It was rather unexpected to find that in both experiments there developed in the men under observation a greater incidence of infection than that found in the random group at the beginning. It had been thought that the greater consciousness of foot hygiene on the part of the men assigned to the experiment might lower the rate of infection. On the other hand, the men in the experiment were observed repeatedly for infection throughout the warmest season, while those in the random group were examined only once and chiefly in the spring.

## PROPHYLAXIS OF DERMATOPHYTOSIS

The results of the use of the various agents are summarized in the three tables.

## TREATMENT OF DERMATOPHYTOSIS

At Haiti's Island during the summer of 1945, 70 men in whom the two feet showed an equal degree of infection were treated with the undecylenic acid-undecylenate ointment on one foot and the unde-

cylenic acid-undecylenate powder on the other. In 15 men the feet treated with the ointment healed on the average one week quicker than those treated with a powder. In 9 men the feet treated with the pow-

TABLE 1—*Experiment I, at Hart's Island, New York (Summer 1944)*

Foot	Preparation Used	Feet, No	Infections	
			No	%
Right	Undecylenic acid-undecylenate powder	137	1	0.7
Left	Boric acid-salicylic acid powder	137	15	10.9
Right	Undecylenic acid-undecylenate powder	144	2	1.4
Left	Sodium propionate powder	144	7	4.9
Right	Boric acid-salicylic acid powder	114	13	11.4
Left	Sodium propionate powder	114	4	3.5

TABLE 2—*Experiment III, at Hart's Island, New York (Summer 1945)*

Group	Series	Foot		Feet, No	Infections, No	Infection, %
I	A	Right	Undecylenic acid-undecylenate powder	107	6	5.6
		Left	No treatment	107	51	47.7
	B	Right	Undecylenic acid-undecylenate powder	106	4	3.8
		Left	Calcium propionate powder	106	8	7.5
	C	Right	Undecylenic acid-undecylenate powder	103	7	6.5
		Left	Talcum powder	103	25	23.1
	D	Right	Undecylenic acid-undecylenate powder	107	4	3.7
		Left	5% thiourea powder	107	21	19.6
	E	Right	Undecylenic acid-undecylenate powder	111	12	10.8
		Left	Foot powder, U S N	111	26	23.4
II	F	Left	1% and 3% iodoform powder	118	5	4.2
		Right	No treatment	118	18	15.3
	G	Right	Foot powder, U S N	119	1	10.9
		Left	No treatment	119	34	28.6
	H	Right	Calcium propionate powder	105	16	15.2
		Left	No treatment	105	49	46.7
	J	Right	5% diodoquin powder	82	2	2.4
		Left	No treatment	82	12	14.6

TABLE 3—*Experiment II, in Florida (Summer 1945)*

Agent Used (Both Feet)	Men No	Incidence of Infections		Reduction of Incidence of Infection, %
		No	%	
No prophylactic agent	1384	387	28.0	Control
Undecylenic acid-undecylenate powder	1,213	48	4.0	83.7
Calcium zinc propionate powder	814	64	7.9	71.8
Boric acid-salicylic acid powder	648	98	15.1	46.1
Sodium propionate powder	105	20	14.8	47.1

der healed on the average one and one-third weeks earlier than those treated with the ointment. In 44 men healing time was the same with both powder and ointment. In 2 men the experiment could not be continued to completion.

In general, the therapeutic results confirmed the finding of the prophylactic series in placing undecylenic acid-undecylenate preparations first among the agents studied. The following figures are abstracted from experiments at Hart's Island and in Florida

Agent Used	Men, No	Cured or Improved, %	Unchanged or Worse, %
Undecylenic acid-undecylenate powder	489	81	19
Sodium propionate powder	164	75	25
Boric acid-salicylic acid powder	221	48	52

#### SUMMARY AND CONCLUSIONS

1 Intensive investigations by the Hart's Island method of paired comparisons, followed by extensive clinical trial on a large group of men in subtropical areas, were employed to ascertain the relative efficacy of various agents in the prevention and treatment of fungous infections of the feet

2 In one large clinical study, the prophylactic use of undecylenic acid-undecylenate powder was found to reduce the incidence of dermatophytosis by 85 per cent

3 The following nine agents were compared as to relative prophylactic efficacy. They are listed in approximately descending order of the efficacy found

- 1 Undecylenic acid-undecylenate powder
- 2 Diodoquin, 5 per cent talcum powder
- 3 Vioform, 1 to 3 per cent in talcum powder
- 4 Calcium-zinc propionate powder
- 5 Sodium propionate powder
- 6 Foot powder, U S N
- 7 Boric acid-salicylic acid powder
- 8 Talcum powder
- 9 Thiourea, 5 per cent in talcum powder

4 Therapeutically, undecylenic acid-undecylenate powder was slightly more effective than sodium propionate powder, which in turn was definitely more effective than the boric acid-salicylic acid powder

5 Therapeutically, there was no significant difference between the efficacy of undecylenic acid-undecylenate powder and undecylenic acid-undecylenate ointment

6 Approximately one quarter of all the men studied and examined had clinical evidence of active fungous infection of the feet

## Clinical Notes

### USE OF THE PURPLE X BULB IN DIAGNOSIS OF FUNGOUS DISEASES OF THE SCALP

CHARLES C DENNIE, M D, and DAVID B MORGAN, M D  
KANSAS CITY, MO

A suitable substitute has been found for the ordinary glass Wood filter. The latter is advantageous in the diagnosis of fungous infections, especially those of the scalp. The substitute is a 250 watt light bulb with nickel and cobalt incorporated in the glass wall of the tube, which thus supplies radiation near the longer wavelength ultraviolet bands. It is made by the General Electric Company. This bulb was designed for the testing of minerals, paints and certain inks that have fluorescing properties. It is known as number 250 A-21-60 natural red purple, Purple X bulb. It sells for \$1.25, and, although the filaments are fragile and may be broken easily in shipment, each intact bulb will last for at least fifty hours of intermittent use. It also has the advantage of fitting any medium light socket designed for 115 volts and operates on either alternating or direct current. However, since the filament operates at a high temperature, the lamp should be used only in a porcelain socket and should never be placed in contact with combustible materials. For protection of the patient and operator, a reflector should cover one half of the bulb and a wire mesh screen can be placed over the open side of the lamp and attached to the reflector. Thus, all that one needs is a small, floor type lamp stand which can be bent in any desired direction and a small dark room.

Microsporon infections of the scalp stand out vividly as a greenish phosphorescence on illumination with this bulb, almost identical in color with that seen with a true Wood filter. The extent of tinea versicolor may also be readily established. To date we have not had any experience with endothrix or leptothrix infections.

Because of the ease of manipulation of this bulb and its low cost, we feel that it will be found most convenient for all dermatologists to have at their disposal, either in their own offices or in clinics. Many physicians do not employ either the Wood filter glass or the filtered ultraviolet lamps that are now on the market. The former is cumbersome because it must be attached to an ultraviolet light by a black canvas focusing cloth, while the latter are expensive compared with the light we have described. Commercial lamps used for indoor photography also provide a source of ultraviolet irradiation, but for this use again a Wood filter attachment is necessary.

These Purple X bulbs can be economically placed in schools for diagnosing or ruling out ringworm of the scalp and can be operated by the school nurses. Private patients with tinea capitis, living at a great distance, can buy one of the bulbs for use in their homes, particularly when there are several children in the family. It is easy to teach the parents the use of this light, in order that they may follow the patient's progress.

A standard 100 watt ultraviolet projector lamp has been compared with this bulb, and the latter has been found just as efficient in producing fluorescence in the several instances of tinea capitis in which both types of lamps were used. In the examination of treated patients, final determination of cure has been the same with both lamps. We cannot be too emphatic in stressing the value of filtered

ultraviolet irradiation as a most necessary criterion for final determination of cure of tinea capitis. It is also felt that three examinations, with normal results, at weekly intervals are necessary to be certain that cure is complete.

Dr. Ralph Mueller, of Kansas City, Mo., an orthopedic surgeon, suggested the use of this lamp, as he has used it in crystallography, his avocation.

1524 Professional Building

## POSSIBLE BENEFIT FROM PROTEIN HYDROLYSATES FOR EXFOLIATIVE DERMATITIS

NORMAN R. GOLDSMITH, M.D., LANCASTER, PA.

This observation is submitted in the hope that it may initiate study and verification by physicians who have access to more clinical material than I.

I am reporting 2 cases of chronic generalized exfoliative dermatitis in which the patients appeared to improve from oral therapy with amino acids after usual measures had failed.

### REPORT OF CASES

CASE 1—The skin of a white man aged 64 had desquamated for two and a half years. According to him, the attack had started from industrial "oil poisoning" and had resisted all previous attempts at treatment. After fourteen days of ingestion of protein hydrolysate, four months previous to the writing of this paper, he was almost well.

CASE 2—In a white woman aged 28, with a definite history of psoriasis for at least ten years, there developed generalized exfoliation of five months' duration. Six weeks after receiving amino acids orally, she showed large islands of normal skin.

Both patients had had the usual supportive therapy, including intramuscular injections of liver extract and soothing topical applications, but neither seemed to improve until the oral administration of the protein hydrolysates.

It is hoped that others will investigate the possibilities of this new, simple, practical aid for what is so often an extremely difficult therapeutic problem.

# Abstracts from Current Literature

EDITED BY DR HERBERT RATTNER

PALMAR ERYTHEMA—ITS RELATIONSHIP TO PROTEIN DEFICIENCY RICHARD M JOHNSON and HANS H HECHT, *Am J M Sc* **211** 79 (Jan) 1946

Palmar erythema has been described as a familial disorder associated with pregnancy, cirrhosis of the liver, pulmonary tuberculosis, rheumatoid arthritis and a wide variety of other diseases. Its frequency is indicated by the authors' observation of 93 instances of palmar erythema in examination of 1,183 patients. It occurred in all ages of both sexes and in a wide variety of diseases. Hypoalbuminemia occurred in 83 per cent of the patients with palmar erythema and in 62.5 per cent of an unselected group of patients in the same hospital, and this difference was regarded as significant.

Johnson and Hecht do not regard hypoalbuminemia as the cause of palmar erythema, but the findings of palmar erythema in a patient should suggest the probable existence of a protein deficiency.

CHLOROMA—A CLINICO-PATHOLOGIC STUDY OF 2 CASES E. G. GOODMAN and LALLA IVERSON, *Am J M Sc* **211** 205 (Feb) 1946

Chloroma represents a rare form of myeloblastic leukemia in which the cells show an unusual tendency toward tumor formation. Its rarity is indicated by the fact that the 2 instances reported in this paper are the only ones in which the conditions were so diagnosed at Duke Hospital among 226,796 patients. In both instances tumors were the presenting signs, and the clinical course was rapidly downhill. In 1 case, in a 7 year old Negro boy, twelve small, firm, pea-sized, movable nodules developed.

LINCH, St Paul

ONCHOCERCIASIS J. G. SCOTT, *Am J Ophth* **28** 624 (June) 1945

Scott found the following ocular complications in 342 Cameroon soldiers, all of whom were assumed to be infected with *Onchocerca*: punctate keratitis, 61 cases, punctate keratitis with iridocyclitis, 27 cases, and presence of microfilarias in the aqueous of otherwise unaffected eyes, 16 cases. Retrobulbar neuritis, atrophy of the optic nerve and choroiditis occurred rarely. The microfilarias of *Onchocerca volvulus* were the commonest (if not the only) microfilarias to enter the anterior chamber. Their presence was well tolerated. The cause of complications was a toxin (probably filarial and possibly microfilarial). The common occurrence of nonencapsulated filarias (*O. volvulus*) is postulated.

W. ZENTMAYER [ARCH OPHTH.]

ACUTE PORPHYRIA CLINICAL AND PATHOLOGIC OBSERVATIONS MAX BERG, *Arch Int Med* **76** 335 (Nov-Dec) 1945

In an unusual case of acute porphyria, Berg made observations on the status of the capillaries of the skin during the acute attack, noting extreme spasm of the capillaries and evidence of injury to some of the capillaries in the form of aneurysmal dilatation. In addition, definite alterations in gastric contractility were recorded. He states that the bullae arising in the skin as a result of exposure either to sunlight or to direct trauma may be related to the increased permeability of the capillaries, which in turn is the result of the injury to the capillary.

VENOSPASM ITS PART IN PRODUCING THE CLINICAL PICTURE OF RAYNAUD'S DISEASE MEYER NAIDE and ANN SAYEN, Arch Int Med **77** 16 (Jan) 1946

Naide and Sayen point out that physicians do not have a clear concept of what is meant by the term Raynaud's disease, and they discuss some of the outstanding opinions. In 10 patients with Raynaud's disease they thought that the clinical features in only 1 were those produced by arterial spasm alone, in 8 both venospasm and arterial spasm were required to produce the picture, and in 1 venospasm alone was present. In the 4 patients with Raynaud's phenomenon, the symptoms were part of a generalized scleroderma, and in 2 of these patients there was evidence of both venous and arterial spasm. The authors use the term "Raynaud's disease" to describe an exaggerated vascular response to cold and to emotional tension with bilateral, symmetric digital involvement. The term "Raynaud's phenomenon" is reserved for digital vasospasm, secondary to other known pathologic conditions such as scleroderma, arthritis and cervical rib.

The observations of the authors lead to the conclusion that in this group of vasospastic disorders the clinical picture varies depending on the intensity of constriction in arteries and in veins and on the type of vessel in which abnormal constriction predominates. It is emphasized that spasm of the veins as well as of the arteries is present in the majority of these patients. Arterial spasm alone cannot explain the clinical picture in most patients. Naide and Sayen also point out that Raynaud's disease is not rare, the milder forms are fairly common and do not deserve the connotation of seriousness usually associated with the diagnosis, and reassurance is an important part of treatment.

RELATIONSHIP OF BOECK'S SARCOID AND TUBERCULOSIS. REPORT OF A CASE IN WHICH TUBERCULOSIS OF LYMPH NODES WAS ASSOCIATED WITH FEATURES HIGHLY SUGGESTIVE OF SARCOID. JUSTIN R. DORGELOH and PAUL W. TULLY, Arch Path **40** 309 (Nov-Dec) 1945

A 9 year old child had painless cervical adenopathy with redness of the adherent overlying skin. There was no cutaneous reaction to old tuberculin or purified protein derivative. The patient also had hyperglobulinemia. Excision was performed, and the sections showed both tuberculoid structure and fairly characteristic sarcoid reaction. Because of the pathologic changes, hyperglobulinemia and anergy to tuberculin, the authors state that this case lends additional weight to the argument that sarcoidosis, in some instances at least, is an atypical reaction to tubercle bacilli or their products.

SCIEREMA ADIPOSUM NEONATORUM OF BOTH INTERNAL AND EXTERNAL ADIPOSE TISSUE. PEARL ZEEK and ETHEL MAE MADDEN, Arch Path **41** 166 (Feb) 1946

There is a generally accepted opinion that subcutaneous fat necrosis of the newborn and nonsuppurative panniculitis are confined to the external adipose tissues. For this reason Zeek and Madden describe a case with widespread involvement of adipose tissue, both internal and external, with lesions which were histologically typical of subcutaneous fat necrosis of the newborn. No other such case was found recorded in the available literature. Because previous studies have apparently been incomplete, it cannot be stated whether this case represents an exception to a general rule or whether the internal lesions have been missed heretofore.

LYNCH, St. Paul

STUDIES ON POISON IVY AND OTHER DERMATITIS-PRODUCING PLANT PARTS WHEREIN ACTIVE, RESINOUS PRINCIPLES ARE SUSPENDED IN AQUEOUS SOLUTION. MARGARET B. STRAUSS and W. C. SPAIN, J. Allergy **17** 1 (Jan) 1946

Reported observations seem to indicate that more than one toxic substance is present in the ivy plant capable of causing dermatitis venenata in susceptible persons. The same is true of poison oak, poison sumac, primrose and other plants.

The poison ivy extracts available at the present time for testing or treatment by the parenteral route are either alcoholic or oily solutions of an oleoresin of the ivy plant. Each of these extracts has objectionable features.

By a special method, which they describe in detail, the authors prepared an "extract" in an aqueous medium. They found the new product nontoxic and non-irritating and as active as an equivalent dilution of the alcoholic ivy extract. Sensitive patients who were treated prophylactically with this preparation "were relieved by the second to fifth injection." Twelve patients who were treated prophylactically in 1943 with an alcoholic extract, with poor results, were treated with this extract in 1944, "with good clinical results." Sixteen other persons treated in a similar manner in 1945 showed "excellent clinical results."

Guinea pigs were sensitized by one intraperitoneal injection of this preparation, as shown by positive reactions to patch tests with 3 drops of a concentrated solution of this extract or alcoholic ivy extract twenty-one days after the sensitizing injection.

**AN ALLERGIC REACTION FOLLOWING TYPHUS-FEVER VACCINE AND YELLOW-FEVER VACCINE DUE TO EGG YOLK SENSITIVITY** SIMON S RUBIN, *J Allergy* **17** 21 (Jan) 1946

The author reports a case of angioneurotic edema in a 19 year old soldier involving the eyelids, bridge of the nose and both cheeks. The eruption appeared one and one-half hours after he had received inoculations of typhus fever and yellow fever vaccines, and it was associated with blocking of the nose and pain in the chest.

Scratch tests elicited negative reactions to chicken feathers, chicken meat and egg white and a positive (4 plus) reaction to egg yolk. Intradermal tests with freshly prepared extracts gave doubtful reactions to egg white in dilutions of 1:1,000 and 1:10 and a positive (4 plus) reaction to egg yolk in a 1:1,000 dilution. Passive transfer tests elicited a negative reaction to egg white, a positive (3 plus) reaction to egg yolk, a positive (1 plus) reaction to yellow fever vaccine in a 1:100 dilution and a positive (2 plus) reaction to typhus vaccine in a 1:100 dilution.

The patient had not eaten whole eggs since infancy because they caused him to vomit, he could eat the white of hard-boiled egg without any trouble. For the past eight years he had had early and late hay fever.

The author concludes that the allergic manifestations were due to sensitivity to egg yolk and calls attention to the allergic potentialities of these vaccines.

**ANAPHYLACTIC SHOCK FROM SKIN TESTING—TWO CASES—ONE FATAL** OSCAR SWINEFORD JR, *J Allergy* **17** 24 (Jan) 1946

The author reports 2 cases of anaphylactic shock from intracutaneous tests with food extracts. One case terminated fatally. The food which caused the fatal reaction was not determined, the nonfatal reaction was thought to be due to mustard.

In each case, anaphylactic shock occurred before the cutaneous reaction was fully developed.

**CONTACT DERMATITIS DUE TO ACE ADHERENT** ANDREW G FRANKS, *J Allergy* **17** 112 (March) 1946

The author observed 4 cases of contact dermatitis due to "Ace Adherent," a preparation employed to obtain skin traction in amputees. The dermatitis (scaly, erythematovesicular) was confined to the area where the adherent was applied. In 1 case, a generalized urticarial eruption followed the appearance of the local reaction.

A patch test with the "Ace Adherent" elicited a "severe reaction necessitating the removal of the test material after four hours."

The ingredients of Ace Adherent include Galex (a dehydrogenated rosin), Venice turpentine, tannic acid, gum camphor and ethyl alcohol. The author suspects Galex as the cause of the dermatitis. MENDELSON, New York

HOSPITAL MORBIDITY AND MORTALITY OF INFANTILE ECZEMA STEPHAN EPSTEIN,  
J Pediat **26** 541 (June) 1945

The occurrence of severe complications and even of death among infants hospitalized because of infantile eczema has led to repeated warnings that children with eczema should not be admitted to a hospital but should be taken care of at home or at a foster home. The author presents a report on 100 consecutive infants with eczema admitted to a hospital from 1937 to 1944. In this series no deaths occurred. Of these 100 children, 21 suffered from twenty-three complications, and there was a morbidity of 21 per cent. A breakdown of these statistics shows that all but one of the complications occurred among the 78 children with atopic eczema and one among the 22 with nonatopic eczema. Nearly all complications were infections of the respiratory tract or gastrointestinal disturbances. They are explained by the author as exacerbations of concomitant respiratory or gastrointestinal allergy. These statistics demonstrate that with the advent of sulfonamide compounds and with proper nursing care there need not be fear of death in hospitalized infants with eczema.

This conclusion should not lead to indiscriminate hospitalization of patients with infantile eczema, but it should eliminate fear in the instances in which the severity of the eczema or other circumstances make hospitalization mandatory.

The so-called sudden death from eczema is discussed. A hypothesis of toxic effects from phenol-like tar products, in combination with interference with cutaneous respiration and disturbance of the autonomous nervous system, is suggested to explain this phenomenon. A reminder is given about the toxicity of coal tar, and it is suggested that tar preparations should not be used over too great surfaces.

AUTHOR'S ABSTRACT [AM J DIS CHILD]

PITYRIASIS RUBRA PILARIS AND VITAMIN A ARTHUR D PORTER and E W  
GODDING, Brit J Dermat **57** 197 (Nov-Dec) 1945

A case is reported of pityriasis rubra pilaris in which there was improvement following therapy with vitamin A. In attributing improvement to vitamin A, the authors realize that it is unwise to draw conclusions from a single case, especially in a disease which is apt to undergo spontaneous remissions.

While it cannot be maintained that pityriasis rubra pilaris is purely a deficiency disease, yet the clinical and histologic appearance of the skin, the therapeutic effect of large doses of vitamin A and the dark-adaptation tests do indicate that vitamin A is implicated at some stage.

The various factors that might be concerned include intake, absorption, conversion of carotene to vitamin A, storage, circulation levels, synthesis of vitamin-protein compounds required by different tissues (e g, photochemical pigments) and the ability of the tissues themselves to utilize these compounds.

The cause of the disease in regard to vitamin A remains at the moment largely speculative. Whatever the cause, it appears that liability to the disease is inherited.

THE FUTURE OF B P OINTMENTS A R G CHAMINGS, Brit J Dermat **58** 1  
(Jan-Feb) 1946

The author considers four main types of skin which should be considered with respect to any particular form of medication: (1) the average greasy skin, with a normal moisture content, (2) the dry though greasy skin, (3) the moist skin, characterized by excessive sweating, and (4) the exceedingly dry skin, defective in both moisture and grease content and readily susceptible to pathologic conditions.

The four general states of the skin enumerated should not be treated with the same base. When the principle is accepted that in general a water-containing medium should be applied to the skin, it would seem that for three of the conditions specified an oil in water emulsion would be desirable, while for the others—the excessively moist skin (no 3)—the water in oil type would be indicated. The latter is at present represented by hydrous ointment prepared from ointment of wool alcohols B P, on which work is presumably still being carried out in order to produce a more satisfactory preparation. For the oil in water base, one prepared with Lanette wax SX would appear to be preeminently satisfactory.

A greasy base should still be included in the pharmacopeia, and white ointment is as good as any, though its emulsifying tendency would perhaps be obviated by the use of hydrous instead of anhydrous wool fat.

BLUFFARD, Chicago

REPORT OF FORTY-EIGHT CASES OF MARGINAL BLEPHARITIS TREATED WITH PENICILLIN. M. E. FLOREY, A. M. MCFARLAN and I. MANN, Brit J Ophth 29 333 (July) 1945

Forty-eight patients with blepharitis were treated with local application of penicillin ointment containing 600 to 800 units of penicillin per gram of base. *Staphylococcus aureus* was isolated from the lesions of 39 of 41 patients examined bacteriologically. Thirty-six of the patients applied their ointment regularly three or four times a day for as long as it was considered necessary (i.e., three to ten weeks). Recovery took place in all these patients without removal of other foci of infection or any adjuvant treatment other than epilation of a few lashes. Bacteriologic observations were found to be closely associated with clinical signs, but the disappearance of *Staph. aureus* from cultures of material from the lids was considered a better indication for cessation of treatment than clinical signs, as it invariably succeeded clinical improvement. A follow-up study a year after treatment was discontinued revealed that two thirds of the patients reporting had remained free of recurrence without further treatment.

W. ZENTMAYER [ARCH. OPHTH.]

STUDIES IN DENERVATION. J. DOUPE and Associates, J. Neurol. & Psychiat. 6 94 (July-Oct) 1943

*Methods*—Doupe and his co-workers carried out a number of investigations on patients with lesions of the peripheral nerves. The methods used consisted in measurement of the peripheral circulation by means of recording cutaneous temperatures of the finger pads, supplemented in some instances by plethysmographic records of the digits. Various measures to modify the circulation, such as local effects of moderate to extreme cold or heat and injections of epinephrine, were used.

*The Circulation in Denervated Digits*—Investigations were carried out to test the validity of the hypothesis of Lewis and Pickering that sympathectomized limbs stay warm while denervated digits become cold. Observations were made on subjects with preganglionic and ganglionic sympathectomies and on subjects with lesions of peripheral nerves. Doupe concluded that contrary to the results of Lewis and Pickering, the digital vascular reactions are similar in the two groups of patients. The cause of the usually diminished circulation in denervated digits is sensitization to cold produced by degeneration of the sympathetic fibers. This sensitization is made the more manifest by the action of circulating epinephrine by the action of vasomotor fibers still supplying the limb and by variations in local and general blood pressure. Part of the difference in the state of denervated and ganglionectomized digits may be ascribed to the persistence in the latter of some postganglionic fibers. The reactive hyperemia which has been observed in denervated digits is in part mediated by arteriovenous anastomoses, is not dependent on any neural mechanism, is greatly slowed by a high sympathetic vasoconstrictor tone and is not affected by the vasoconstriction caused by cooling the denervated digit. Denervated blood vessels appear to be histologically normal.

There is no correlation between Raynaud's syndrome and sensitivity associated with denervation. In the former condition there is no hypersensitivity to epinephrine. In the latter there is no history suggestive of vasospasms, the cyanosis is slight and there is a ready response to reactive hyperemia. Thus, with lesions of peripheral nerves the blood flow is adequate to the needs of the tissue, while with Raynaud's syndrome ischemia occurs. The trophic changes in denervated digits are attributed to the lowered tissue metabolism consequent on the persistent coldness, since the blood supply is adequate. The sensitivity to cold in denervated digits may be explained on the basis of changes in hydrogen ion concentration, since a fall of temperature would directly raise the  $p_H$  and produce vasoconstriction or decrease the formation of acid metabolites and thus indirectly lead to elevation of the  $p_H$  and vasoconstriction. The regain of tone following denervation is ascribed to the action of local influences on sensitized vessels. A circulating vasoconstrictor substance in the blood may only be assumed in the case of systemic disorders.

*Inflammation and Trophic Ulcers in Denervated Areas*—Slow healing of trophic ulcers produced by burns or pressure in denervated digits has been ascribed to diminished blood supply. Since the authors contend, however, that the blood supply of denervated digits is adequate, there must be other causes for the delayed healing. In the case of ulcers following burn, the slow healing is only apparent, since data are lacking on the extent of the original trauma because of loss of pain sensation in the denervated area. In the case of ulcers produced by pressure, slow healing is due to edema associated with impairment of the lymph drainage in the extremity. The occasional presence of a vesicular eruption in cases of peripheral nerve lesions also is due not to denervation but to a variety of cheiropompopholy.

*Mechanism of Axonal Vasodilation*—On the basis of a case of section of the ulnar nerve, Doupe concludes that axonal vasodilation is mediated by fibers other than those associated with sensation. The mechanism of axonal vasodilation is still obscure. According to Lewis, it depends on efferent cholinergic fibers having their trophic center in the posterior root ganglions and distributed in the skin in the form of a plexus, stimulation of which releases the so-called H substance. A review of the literature fails to corroborate this view. The author offers an alternate hypothesis, viz., that the fibers subserving axonal vasodilation are afferent and that they terminate in a branching axon system with receptors specially sensitive to products of tissue damage, similar to histamine. Axonal vasodilation is thus attributed to the metabolites of nerve fibers rather than of cells of the skin.

*Epinephrine*—Denervation of digital vessels in human subjects renders them hypersensitive to the vasoconstricting action of epinephrine. This is due to degeneration of sympathetic fibers, which produces in the vessels of denervated digits a lowered threshold and a prolonged response to the action of epinephrine. The vessels of preganglionectomized digits, on the other hand, show only a lowered threshold. This difference between degenerative and nondegenerative section of sympathetic nerves is due to a loss of "accommodation" in the former which is not present in the latter. Emotional stimuli cause a release of epinephrine in the body, but the need for heat conservation is a more variable and less constant cause of such liberation. Thus, the original view of Cannon that secretion of epinephrine is associated with mental excitement is more correct than his later assumption that epinephrine participates in many of the ceaseless variations in body function. Peripheral neurogenic vasoconstriction is not necessarily accompanied with the release of epinephrine, an indication that within the sympathico-adrenal system different patterns of behavior are elicited by stimuli of different types. Epinephrine could be liberated in the body in amounts comparable to the rapid intravenous injection of 2 micrograms or to injection of the drug for longer periods at the rate of 6 micrograms per minute. In other circumstances much larger amounts might be liberated, which would suffice to initiate persistent vasoconstriction in a denervated digit.

*Circulation in the Skin of the Proximal Parts of the Limbs*—Doupe and his collaborators confirmed the view expressed by Grant and Holling that there exists a vasodilator sympathetic supply to the blood vessels in the skin of the proximal parts of the limbs by producing active vasodilation in response to intense heating of the body. The lack of effect of nerve block when the subjects are cold shows that there is no significant vasoconstrictor innervation of the vessels in these areas of the skin. The vasodilation is not dependent on the activity of the sweat glands, since the action of the latter can be abolished by atropine without thereby decreasing the vasodilation. The thesis of Grant and Holling is not refuted by the occurrence of vasodilation following sympathectomy. The latter phenomenon may be due to discharges in vasodilator fibers, which are decentralized by the operation, to the anesthetic and to absorption from traumatized tissues.

*Sebaceous Secretion*—The author and his co-workers estimated the sebaceous secretion in a subject with a sympathectomy and in another subject with a lesion of the brachial plexus. They found that the sebaceous glands can function in the absence of all nerve fibers. Similarly, the growth of hairs and the metaplasia of the cells of the epidermis are unaffected by deprivation of direct nerve influences. Sebaceous secretion is thus simply a manifestation of the growth of the cells of the sebaceous glands. The physical state of the skin influences the production and absorption of the sebaceous material. The abundant secretion in cases of lethargic encephalitis may be due to disturbances in hormonal regulation.

*Effect of Electrical Stimulation on the Circulation and Recovery of Denervated Muscle*—The value of electrical treatment of denervated muscles was investigated in a series of 12 patients after suture of the musculospiral or the posterior interosseous nerves. It was found that electrical treatment had no beneficial effects on the return of motor power. This failure was ascribed to the fact that the treatment does not impose a strain on the muscles of sufficient intensity to be of therapeutic value. The amount of electrically induced exercise was estimated by using the rate of blood flow as an index, and it was found that even more intensive stimulation produced a relatively slight increase in blood flow. The only benefit derived from electrical therapy is in induction and reeducation of muscular movements.

*Contractility and Excitability of Denervated Muscle*—The electrical reactions of denervated muscles consist in changes in contractility and excitability. Repetitive excitation is likely to develop in denervated muscle when it is subjected to an electric current. This phenomenon is a persistence of potentials throughout the phase of muscle shortening, due to the fact that each muscle fiber is responding more than once. It is readily produced by a constant current. The phenomenon of galvanotonus is also attributed to the repetitive firing of the muscle fibers. Denervated muscles usually show prolonged contraction, which is due to repetitive stimulation by constant currents in conjunction with a cool state of the muscle. Similarly, denervated muscles show prolonged excitation, which is also due to repetitive stimulation plus the relation of the muscle fibers to the field of the current. Electrical reactions are of clinical value only when positive, for when negative they may be attributed to factors other than the state of degeneration of the muscles.

MALAMUD, San Francisco [ARCH NEUROL & PSYCHIAT]

FAVUS C. H. WHITTLE, Proc Roy Soc Med 38 229 (March) 1945

A case of favus in a boy of 6½ years is reported. The condition was diagnosed as psoriasis when the child was first seen, because of the absence of fluorescence under the Wood light, but on examination some of the hairs and scales were found to contain abundant fungous elements, chiefly coarse branching hyphae.

WILLIAMSON, New Orleans [AM J DIS CHILD]

# Society Transactions

## NEW ENGLAND DERMATOLOGICAL SOCIETY

Bernard Appel, M D, *President*

G Marshall Crawford, M D, *Secretary*

*April 11, 1945*

Xanthoma Disseminatum (also Tuberosum et Planum) Presented by  
DR JOHN G DOWNING, Boston

F C, a 44 year old white man of Irish-American descent, was presented from the Massachusetts Memorial Hospitals. Five years ago the patient noted the appearance of yellowish lesions on the palms and a yellowish tint in his eyes. The lesions gradually became generalized. Some loss of weight and fatigue were also apparent. Three years ago an examination revealed an enlarged liver. For the past year the yellowing of the skin has been progressive. The urine has been dark, and from five to six light brown stools have been passed daily. He has been increasingly fatigued.

At this time the patient presents deep jaundice of the skin, mucous membranes and scleras. Numerous nevi aranei are seen on the upper part of the trunk and the neck. The palms, flexor creases of the fingers, cubital fossae, axillary folds, neck, face and eyelids reveal multitudes of small, flat, pale yellow papules. In the axillary areas these have coalesced. Pinhead-sized papules are diffusely scattered over the remainder of the surface of the skin, with coalescence at pressure areas. These are most profuse on the extensor surfaces of the forearms. On both elbows there are nodular lesions, approximately 1 cm in diameter. The liver is tremendously enlarged (the edge was palpable 10 to 12 cm below the right costal margin in the midclavicular line), firm and nodular. The spleen is also moderately enlarged.

Laboratory findings were as follows: serum bilirubin content, 19.32 mg per hundred cubic centimeters, icteric index, 75, and alkaline phosphatase level, 56 King-Armstrong units (normal 7 to 14). The urine contained bile (4 plus). The total cholesterol content amounted to 447 mg, and the cholesterol esters to 250 mg per hundred cubic centimeters.

### DISCUSSION

DR WALTER F LEVER: I think that it is of interest that the cutaneous lesions preceded the jaundice in this patient. As far as I know from the literature, in most cases jaundice precedes cutaneous lesions, often by many years. It has been a much discussed question whether hepatic disease can cause xanthomatosis or whether the xanthomatosis is primary and the hepatic disease secondary. A case like this would favor Thannhauser's contention that the xanthomatous disease is primary and the biliary cirrhosis secondary, due to xanthomatous deposits in the bile ducts.

DR BERNARD APPEL: The diagnosis is primary essential xanthomatosis of hypercholesteremic type with secondary biliary cirrhosis. That is the type that Thannhauser classifies as xanthoma planum et tuberosum.

DR JOHN G DOWNING: Eusterman and Montgomery (Eusterman, G B, and Montgomery, H. Disorders of Liver and Extrahepatic Biliary Ducts Associated with Cutaneous Xanthomas and Hyperlipemia, *Gastroenterology* 3:275 [Oct] 1944) reported a fatal case of the condition occurring in a woman 48 years of age seen at Mayo Clinic. She showed all the physical signs of the patient exhibited today. She also had severe hyperlipemia. They stated the belief that this is consistent with Thannhauser and Magendanz' concept of essential xanthomatosis.

as seen in so-called xanthomatous biliary cirrhosis. The authors stressed that cutaneous xanthomatosis and hyperlipemia occasionally occur in association with primary disease of the liver (so-called xanthomatous biliary cirrhosis) and in association with hepatic disease that is secondary to obstruction of the common bile duct, especially as the result of postoperative stricture. In cases in which the hepatic disease is primary the prognosis is generally unfavorable. It is more favorable in cases in which the underlying pathologic process is due to obstruction of the common duct.

#### Xanthoma Disseminatum Presented by DR JOHN G DOWNING, Boston

M F B, a 48 year old white woman, is presented from the Massachusetts Memorial Hospitals.

Her illness began three years ago with generalized pruritus, progressive yellowing of the skin, loss of weight and frequent epistaxis. Two years ago she noted discrete yellow lesions on her eyelids and forearms, following which the eruption became more widespread. Within the past year there has been no discernible change in the jaundice or cutaneous manifestations, but the patient has had three severe hemorrhages from the gastrointestinal tract. The site of bleeding has not been determined.

A deep jaundice is evident throughout the patient's skin, mucous membranes and scleras. The palms, cubital spaces, axillas, neck and eyelids reveal multiple plaques of assorted sizes which are composed of coalesced, slightly raised, flat-topped, pale yellow papules. On the anterior aspects of the thighs, discrete yellowish papules of a follicular type are found. The liver is greatly enlarged, firm and nodular. The spleen is not palpable.

The laboratory findings were as follows: serum bilirubin content 16.3 mg per hundred cubic centimeters and alkaline phosphatase content 45 King-Armstrong units. The total cholesterol level amounted to 500 mg per hundred cubic centimeters. The urine contained bile (4 plus).

#### DISCUSSION

DR GEORGE E MORRIS: I should like to suggest that this patient is suffering from xanthoma eruptivum and xanthoma diabeticorum. She has lesions which are red and pruritic on her legs, which is not xanthomatosis of the tuberosa type.

DR WALTER F LEVER: Patients with primary xanthomatosis of the hypercholesteremic type may have secondary xanthomatosis, or the eruptive form of xanthomatosis, which is due to lipemia. It is often referred to as xanthoma diabeticorum, but this is not a correct designation, because not hyperglycemia but the hyperlipemia frequently associated with diabetes causes the lesions. Frequent epistaxis and gastrointestinal bleeding may be due to a deficiency in vitamin K. I remember a case of primary xanthomatosis that came to autopsy two months ago. The patient had originally come into the hospital because of uncontrollable epistaxis. The only way of stopping the bleeding was by giving large doses of a preparation of vitamin K intramuscularly and orally, which helped as long as it was given.

DR MALCOLM STANLEY (by invitation): If I may review briefly his classification, Thannhauser divided the disease into primary, or essential, xanthomatosis and secondary xanthomatosis. The secondary type is associated with hyperlipemia, oftenest due to uncontrolled diabetes, occasionally von Gierke's (glycogen storage) disease and rarely familial hyperlipemia. The last is characterized by different types of xanthoma, particularly the kind which was called xanthoma eruptivum, which both these patients have, or have had, and which is believed to be due to the hyperlipemia with biliary obstruction. The serum in these cases is of differential diagnostic significance, milky in the secondary varieties and clear in the essential types.

The primary, or essential, types are divided into three classes: the hypercholesteremic, the normal cholesteremic and a combination of the two. The hyper-

cholesteremic type is characterized, according to Thannhauser<sup>1</sup>, by xanthoma planum et tuberosum, tendon xanthoma, xanthoma of the coronary arteries and the vascular system in general, xanthoma of the biliary system and xanthoma palpebrarum. The normal cholesteremic type is characterized by xanthoma disseminatum, with occasional osseous and pulmonary involvement, there are no tuberous xanthomas and no involvement of the tendon sheaths, coronary arteries or biliary tract. I believe that the distribution of these (disseminate) lesions is particularly on the flexor surfaces, as today's patients have shown, in the axillas and on the neck. Then there is the third type, the combination of the two.

The 2 patients who are shown here have xanthomatosis of the essential hypercholesteremic type, with blood cholesterol values in the neighborhood of 500 mg per hundred cubic centimeters (normal 150 to 200 mg) and a clear serum. Both patients, however, show cutaneous lesions of all types (planum et tuberosum and disseminate and eruptive varieties of xanthoma), both primary and secondary, and both have biliary cirrhosis. In the second patient the jaundice came on before the xanthomas were seen by her. She had three severe gastrointestinal hemorrhages. In both cases the prothrombin time has always been within normal limits. It is well known that these patients have epistaxis. Gastrointestinal hemorrhages are better explained by xanthomas in the tract itself. In dogs, if the common bile duct is tied, ulcers will appear in the duodenum at the level of the ampulla of Vater. This does not apply in the present instances, since there is obviously plenty of bile getting into the duodenum, as determined by the normally pigmented stools. Another possible explanation is esophageal varices, though they were not demonstrable in the second patient. She has had three massive gastrointestinal hemorrhages, and one cannot find out why, all one can do is to give her transfusions.

To speak for a moment about the biliary cirrhosis, the woman has definitely xanthomatous biliary cirrhosis, proved by operation, biopsy and cholangiogram. It is known, therefore, that the jaundice is not due to extrahepatic obstruction. The man has not had proof by biopsy, although I think that he falls into the same category. His stools are of normal color. He has no other evidence of extrahepatic obstruction.

These cases are presented from the standpoint of being interesting to the general practitioner because of the widespread systematic disease and to the dermatologist because of the striking dermatologic pictures which are the outstanding manifestations. The prognosis is poor in both the cases.

#### A Case for Diagnosis (Syphilitic Glossitis?) Presented by DR JOHN G DOWNING, Boston

J L, a 73 year old white man, has complained of a sore mouth and tongue for two years. This has been an intermittent disturbance of irregular occurrence. In 1942 he was found to have a positive reaction to a serologic test of the blood for syphilis.

The anterior portion of the tongue is distinctly atrophied. There are a few superficial ulcers along the sides. The buccal mucous membranes and the dorsum of the tongue are covered with patches of a grayish white exudate which is not easily removed.

A culture planted with material from the mouth has shown no growth of fungus.

Treatment has consisted of potassium iodide by mouth and a mouthwash of sodium perborate.

#### DISCUSSION

DR JACOB H SWARTZ. It seems to me that this man has a degenerative process superimposed on a syphilitic base.

DR FRANCIS M THURMON. There is an element of avitaminosis which is superimposed on a syphilitic background. When the left margin of the tongue was palpated, there was a certain amount of induration suggestive of an early

stage of a malignant growth. Submaxillary and submental glands were not palpable. Intraoral cancer, especially of the tongue, in a patient with tertiary syphilis does not respond to treatment. It usually requires six to nine months for the fatal outcome, despite any and all types of therapy used. A histologic examination of the lesion of the tongue should be made.

DR JOSEPH MULLER. Suggestions for therapy were requested. I should say that there is definitely a possibility of a malignant growth, but the proper procedure would be to give him adequate antisyphilitic therapy and plenty of vitamins first and suspend decision on further steps until one sees if he has a cancer. Let the two things which are visible be treated.

DR GEORGE E. MORRIS. There is a group of syphilologists who believe that a patient with a tongue such as this should not receive arsenotherapy. How do the members feel about this?

DR FRANCIS M. THURMON. In the past two years I have seen 3 cases like this. Each has been fatal, each patient had intensive therapy for syphilis, and it accomplished nothing.

DR WALTER T. GARFIELD. I can recall 2 similar cases. In the 1 the patient was a woman who had had syphilis years ago as a girl and had some treatment. Later a dentist discovered this condition in her mouth, and she was referred to me. A serologic test of the blood for syphilis elicited a positive reaction. I gave her the regular treatment of arsenic and bismuth compounds, the lesion on the tongue did not clear, but it did improve. She lived for ten or fifteen years longer, the last time I saw her she was 80 years old. In the other case the patient was a man whom I treated eight or ten years ago, he is still alive and active.

DR FRANCIS M. THURMON. Did Dr. Garfield have biopsies done?

DR WALTER T. GARFIELD. No.

DR WILLIAM P. BOARDMAN. I thought that this was a case of leukoplakia but there is certainly degeneration on the left side of the tongue. I recommend a histologic examination. Leukoplakia does not improve with antisyphilitic treatment.

DR C. GUY LANE. One thing which impressed me is the fact that this man had potassium iodide for an unstated period without response. How long did he take it?

DR BERNARD APPEL. It was not long, and the dose was not large—30 drops daily.

DR C. GUY LANE. I should not think that a fair test on which to make any estimate of response to treatment. I feel that there is syphilis present. This impresses me as a manifestation of late syphilis, and I should give him an adequate trial with chemotherapy. I should be inclined to begin with potassium iodide and a bismuth compound or mercury. I should not hesitate to give him arsenic. I believe that a leukoplakic area should be examined histologically. The patient should have an adequate vitamin intake. A hunt for Monilia was made, but I think that nothing was found. The cultures were sterile.

DR JOHN G. DOWNING. I saw this patient yesterday, and the members may be interested in the orders for treatment. I had my dental consultant see him also. He is being sent into the hospital first to have the dental caries relieved, second, to undergo histologic study and third, to receive a full course of penicillin and large doses of vitamins. I think that the condition in this case is a combination of syphilis with secondary infection of the mouth, the latter may be moniliasis or infection with various pyogenic bacteria. I think that it could come from the carious teeth and the pyorrhea present. Then, with regard to the possibility of a malignant growth, I could not find any evidence of one yesterday. The leukoplakia may improve with this therapy. I do not agree with Dr. Thurmon. I think that a man who has had this for two years may improve a great deal. I have seen this type of leukoplakia last for many years.

DR AUSTIN W CHEEVER Dr Downing has explained this whole situation extremely well I do not see any evidence of cancer It might easily be there or eventually develop I do not think that anything can be accomplished by anti-syphilitic treatment I have seen patients with tongues like this who lived for years I have no objection to giving him treatment, but I should keep it within cautious and reasonable limits

DR EDWARD A LAFRENIERE When this man was first seen, about a month ago, he was worse than he is now, the diagnosis was vitamin B deficiency He was given prescriptions for potassium iodide and sodium perborate The following week he came back worse, and all the prescriptions were in his pocket The next week he returned with some improvement after taking vitamin B complex Material was taken for microscopic examination and culture at that time I definitely saw some filaments of fungi in the smear Since then the picture has not changed appreciably

**A Case for Diagnosis (Tuberculosis Orificialis?) Presented by DR BERNARD APPEL, Lynn, Mass**

M M, a 25 year old American Negro woman, first noticed a growth near the anus three months ago It was mistaken for a hemorrhoid The lesion continued to enlarge and about three weeks ago became painful

There are two extremely tender irregular ulcers of the perineum They extend from the frenulum pudendi posteriorly to the anus and beyond for a short distance, forming a ragged ulcerated area approximately 8 cm by 6 cm The edges are firm and somewhat undermined in some places and granulomatous in others From the ulcer on the left of the anus are two fistulas, one leading into the rectum and the other into the vagina They are difficult to probe and are extremely tender

The Frei test for lymphogranuloma venereum gave negative results A roentgenogram showed that the chest was normal The Volmer tuberculin patch test elicited a negative reaction The Hinton, Wassermann and Kahn reactions of the blood were positive Histologically, this lesion resembled granuloma inguinale, but no leishmania bodies could be demonstrated

No treatment has been instituted

**DISCUSSION**

DR MAURICE J STRAUSS I could not find the slide, but the case report stated that the biopsy had been reported as being consistent with a diagnosis of granuloma inguinale, although no leishmania bodies were found It is not always easy to find leishmania bodies In fact, in a large percentage of cases it is impossible, and I do not feel that this rules out the diagnosis of granuloma inguinale

DR BERNARD APPEL While making the rounds of the wards a few days ago I asked Dr John Foley, who has had experience with tuberculosis, to examine this patient He did so and expressed the opinion that this entire picture was consistent with tuberculous ulcer because of its location, the undermined edges of the ulcer and the entire clinical picture Dr Foley said that he has seen many of these perianal tuberculous ulcers and that this case fits in with the picture

DR MAURICE J STRAUSS It may be of interest to know that when I looked at this patient there was no history of the case available and that one of the possibilities that occurred to me was that this might be tuberculosis I also want to point out that these granulomatous lesions around the anal orifice are most difficult ones on which to make an accurate diagnosis Some of them will show a microscopic picture consistent with tuberculosis and will later on be found to be a foreign body reaction In this particular case there is no evidence that the biopsy showed a picture which looked like either tuberculosis or a foreign body reaction, so I believe that one must be satisfied with the diagnosis of granuloma inguinale

DR WALTER T GARFIELD For my own information, I should like to know how often one finds these tuberculous ulcers around the anus without other tuberculosis. The patients whom I have seen have had tuberculosis above the ulcer. I have not seen any with a normal chest, a negative reaction to tuberculin and no history of tuberculosis at all.

NOTE—Another biopsy report of an examination made about four weeks after the meeting at which the case was presented stated that the condition was consistent with lymphogranuloma venereum. Also, persistent questioning brought out a history of ten months of antisiphilic treatment and a previous positive culture for gonococci. After treatment with 2,800,000 units of penicillin by intramuscular injection of 40,000 unit doses at three hour intervals, there was a dramatic healing of the entire ulcerated area. The two fistulas are still patent.

**A Case for Diagnosis (Multiple Idiopathic Hemorrhagic Sarcoma or Hemangioendothelioblastoma?)** Presented by DR JOHN G DOWNING, Boston

J G, a 57 year old white man, noticed a small dark spot on the dorsum of the left foot seven weeks ago. About five weeks ago two smaller lesions appeared on the right hand and one on the left hand. There have been no subjective symptoms relative to these cutaneous lesions. He was subsequently admitted to the Boston City Hospital with the complaint of a cramplike, diffuse abdominal pain accompanied with nausea, vomiting, chills, fever and sweats.

An examination revealed only lesions of the hand at this time, the original one on the left foot has been removed for study. On the flexor aspect of the third and fifth fingers of the right hand there are lesions 0.5 to 1 cm in diameter. These are slightly raised papules of purplish color. One similar lesion is present on the left palm and is surrounded by a red areola.

A histologic examination of the lesion taken from the left foot showed idiopathic hemorrhagic sarcoma of Kaposi. There was bile (3 plus) in the urine. The non-protein nitrogen in the blood was 35 mg per hundred cubic centimeters, and the serum protein level was 5 mg per hundred cubic centimeters, with an icteric index of 12. The Hinton reaction of the blood was negative. A 2 plus reaction to the cephalin flocculation test was obtained. The Graham test showed faint filling of the dye in the gallbladder and 40 per cent emptying.

The patient has been on a fat-free diet, with symptomatic improvement.

#### DISCUSSION

DR WALTER T GARFIELD I have known this man since perhaps 1921 or 1922. About two years ago he came into my office exhibiting a lesion on the foot which I thought was a hemorrhagic sarcoma of Kaposi. At that time he was attending the Massachusetts General Hospital for his arthritis, and I suggested that he show the staff the lesion and ask them to perform a biopsy. The next time he appeared, it had been removed by another physician. I think that it was probably burned out. No report was obtainable.

DR JACOB H SWARTZ I favor the diagnosis of Kaposi's disease but should like to suggest also the diagnosis of melanoma. I have seen one or two lesions that were diagnosed as Kaposi's sarcoma, but which turned out to be melanoma.

DR WALTER T GARFIELD One should recall that Kaposi's sarcoma is usually symmetric and bilateral. This man has had nothing on his other foot.

DR JOHN G DOWNING Dr Swartz's suggestion is excellent. From a medico-legal standpoint these cases are important. All dermatologists have a tremendous dread of removing pigmented moles. The small nodular lesions on this man's palms suggest systemic disease to me. A history of the removal of a small tumor and the later appearance of other lesions may incriminate the trauma, but one forgets that many of these conditions originate systemically. I am tempted to believe that this case is one of hemangioendothelioblastoma rather than of Kaposi's.

disease If the picture is studied histologically, sarcoma can definitely be disregarded There is increased vascular tissue and little increase in fibrosis In hemangioendothelioblastoma, the primary lesion may be in the liver I think that this man should be studied with that in mind, he does present signs of hepatic disturbance

**Juvenile Acanthosis Nigricans and Ichthyosis** Presented by DR LEON BABALIAN, Portland, Maine

E B, a 22 year old white man, presents a symmetric eruption involving the upper two thirds of the body, which began when he was 3 months old It was said to be a "dirty-looking spot" when it was first seen This spread steadily until it covered most of the trunk, the neck and the upper extremities A few lesions appeared on the thighs when the patient was 6 years old, but they faded away several months later When he was 12 years old, some appeared on the face Since that time there has been no further change in the area of involvement, but the eruption has become progressively rougher, thicker and darker The patient is said to have always been deficient physically and mentally His mother has diabetes She and one other offspring have several moles, but there is no familial history of any eruption similar to that exhibited by the patient

The cutaneous surface is generally rough, dry and thick, is covered with numerous papillary growths and has a dirty brownish hue Scattered over both cheeks are yellow-brown papules the size of millet seeds They are larger on the eyelids, which are furrowed The whole scalp is thick, rough and verrucous in appearance On the neck the papillary growths become confluent, forming dark brown, thick patches with exaggeration of the folds of the skin These areas are sprinkled with pea-sized nodules Excepting these larger excrescences, the same kind of patches are seen on the torso In places they form wide stripes with infrequent thin channels of normal skin between them They are thicker and darker on the nipples and in the umbilical area On the flexor surfaces of the upper extremities and the groins, the patches turn grayish black and pachydermic, with extension movements they appear to be formed of parallel horny ridges separated by deep rugae On the front and back of the penis, there are longitudinal stripes of the same eruption The mouth, hands, feet and legs appear normal There is no change in the hair and nails

A biopsy specimen taken from the neck showed a thickening of the epithelium The basal layer was more prominent than usual, with excessive pigment There was hyperkeratosis, and in places there were keratinized plugs with small epithelized cysts In the corium there were occasional chromatophores filled with pigment The papillae were hypertrophied, elongated and in some places divided There was a mild lymphocytic infiltration in the corium

A roentgenologic examination revealed that the gastrointestinal tract was normal Results of the routine examinations of the blood and urine were within normal limits The Hinton and Kahn reactions of the blood were negative

For six weeks the patient has been taking 200,000 units of vitamin A daily In that time his eruption has faded noticeably on the face and neck

DISCUSSION

DR FRANCIS M THURMON What faded in this case? The lesions are so extensive that improvement must have been minimal From the history, some lesions apparently disappeared spontaneously before the administration of vitamin A

DR ALFRED HOLLANDER Clinically, this case does not appear to me as one of juvenile acanthosis with ichthyosis In the latter disease there should be more hyperkeratotic lesions I think that one should consider this a nevus because the pigmented areas on the abdomen undergo transition from smooth skin to a nevus verrucosus type of lesion Histologically there is one section which looked typical of this diagnosis

DR WALTER F LEVER The histologic section did look like nevus verrucosus. I think that it makes little difference whether one uses the clinical designation nevus verrucosus or ichthyosis hystrix. I think that they are both nevoid and the same thing.

DR FRANCESCO RONCHFSE Nevus verrucosus and ichthyosis hystrix should be considered identical.

DR JACOB H SWARTZ I note that the diagnosis is juvenile acanthosis nigricans with ichthyosis. I think that acanthosis nigricans will cover the whole thing. First of all, the disease came on when the patient was 3 months old. He has definite hyperkeratosis on the nipples. The eruption came first on the neck, where acanthosis of the juvenile type frequently begins. It has the distribution of acanthosis nigricans. I should much prefer to call it juvenile acanthosis rather than ichthyosis.

DR JOHN G DOWNING I disagree with Dr Swartz. Ichthyosis hystrix is a dermatologic entity which merely resembles another in some respects. Juvenile acanthosis nigricans is a separate clinical entity. This eruption is a nevus which is verrucous and should be classified as ichthyosis hystrix. I think that the two entities should be kept distinct.

DR LEON BABALIAN I think that both these diagnoses are correct. The pigmentary and papillary growths scattered all over the body are, according to Darier's description, characteristic of acanthosis nigricans. On the other hand, the hyperkeratotic appearance of many of these areas and their linear disposition fit into the diagnosis of ichthyosis hystrix. The same uncertainties prevail in the pathologic picture, which is one of papillary and hyperkeratotic nevus, but with an abundant amount of pigment that is unusual in ichthyosis hystrix. In the literature the association of acanthosis nigricans with nevoid changes is not rare, and it is my belief that juvenile acanthosis nigricans and nevus are one and the same disease.

What also interested me was that this condition improved with large doses of vitamin A. I am aware that spontaneous remissions can be seen in acanthosis nigricans, but the rapidity of the improvement was surprising after this medication.

**A Case for Diagnosis (Psoriasis, Dermatitis Medicamentosa?)** Presented by DR FRANCIS M THURMON, Boston

S N, a 6 year old white girl, was presented with a generalized eruption of eight days' duration. Two weeks ago a small "pimple" appeared on the lateral aspect of the left leg. This enlarged to form a round, yellowish, crusted lesion 4 cm. in diameter. Eight days ago the eruption became generalized, and additional lesions have continued to appear. Six days ago sulfathiazole was prescribed, a total of 12 tablets was taken. A sulfathiazole ointment was applied two days ago to the area on the left leg. There has been no pruritus.

This eruption is a generalized dermatitis, including the scalp, palms and left sole. It is papulovesicular, with discrete lesions of 2 to 10 mm in diameter. They rest on a red base, and some have acquired a yellowish crust, while others show fine white scales. On the forehead and cheeks and in the popliteal fossae, they have become confluent. There are no oral lesions. A few cervical and submaxillary glands are palpable.

The laboratory findings were as follows. The rapid Hinton reaction of the blood was negative. A urinalysis showed 0.1 per cent sugar, no acetone, no diacetic acid and no sediment. A routine examination of the blood gave results within normal limits except for a 10 per cent eosinophil count in the differential smear.

#### DISCUSSION

DR JACOB H SWARTZ This patient interests me because I have had 2 similar ones in private practice, and I saw 1 or 2 at the Massachusetts General Hospital.

The eruption is psoriasis of the acute type, coming on within ten days after the patient had a sore throat and had received a sulfonamide compound. The diagnosis of psoriasis was confirmed pathologically. In each instance there was reason for giving the drug. Do sulfonamide compounds or infections of the upper part of the respiratory tract precipitate potential psoriasis? There have been too many such instances to be coincidental.

DR ELLWOOD C WEISE That is a keen observation. I have noticed the same thing on 2 occasions, both eruptions occurring in children after a sore throat. In my patients typical guttate psoriasis developed. These cases occurred before the days of sulfonamide drugs, so the drugs could not be blamed. The development of acute psoriasis following an infection of the throat seems to me to be more than coincidental.

DR ALFRED HOLLANDER I have seen 2 cases of this kind. In the first case the patient showed a generalized psoriasis after sulfathiazole was given internally for sore throat, and in the second the eruption developed into generalized psoriasis after an application of sulfathiazole ointment. In the latter case the patient had injured his leg, the resulting abrasion was treated with 5 per cent sulfathiazole ointment. He struck his leg again fourteen days later, psoriasis developed on the site of the injury and became generalized after another two weeks.

DR LEONARD E ANDERSON I recall 2 specific instances in which there occurred rapidly developing guttate psoriasis following an illness with fever when no sulfonamide drug had been used.

DR AUSTIN W CHEEVER I remember 1 patient who had psoriatic papules everywhere that chickenpox lesions had been. In another patient psoriasis developed in subsiding syphilitic lesions. I have seen 2 instances in which psoriasis appeared around or in the scar from vaccination.

DR ELLWOOD C WEISE In this particular case there were no previous cutaneous lesions. The incidents which Dr Cheever and Dr Hollander presented are well known, namely, that previous injury or some change in the skin will determine the localization of the psoriatic lesion. However, in this particular instance there were no previous cutaneous lesions prior to the onset of the sore throat.

DR AUSTIN W CHEEVER I saw 1 girl who had two attacks of psoriasis, twelve years apart, each coming on after tonsillitis before the days of sulfonamide drugs.

DR FRANCIS M THURMON I have always looked on these cases of acute psoriasis as being due not to an acquired factor but rather to the blending of the chromosomes which denote the biologic habitat of each person. Whatever the stimulating factor is, be it drug or trauma or excessive amounts of sunshine, the cutaneous response of psoriasis is always the same. That is what happened in this case, namely, a stimulus played on a certain type of physiologic background, and the response was psoriasis.

DR ALFRED HOLLANDER I believe that this case can be explained by the theory of Koebner's phenomenon.

#### Tertiary Syphilis of the Skin Presented by DR G MARSHALL CRAWFORD, Brookline, Mass

A L, a 49 year old white man, complained of a dry, cracking eruption of the left palm of six years' duration. There have been occasional episodes of bleeding from the area. The eruption gradually spread over the wrist, with the development of red scaly lesions. About a year ago these appeared on the back of the hand. The patient is a cattle dealer, and his hand is subject to considerable trauma. There is no other history of cutaneous disease. The patient said that he had no venereal infection. The marital and general medical histories were noncontributory.

Tests of the blood have been made repeatedly in the past and are said to have given normal results. Several years ago the patient's family physician gave him eight injections into a vein of his arm, the nature of this treatment is not known. There was no improvement in his hand following this therapy.

The left hand reveals diffuse keratosis of the entire palm and the flexor aspects of the fingers, thickening is most pronounced on the palm. There is some fissuring in the flexural folds of the fingers. The keratotic change is rather well defined at the sides of the hands and the fingers. Proximally it thins out at the wrist into an erythematous, slightly scaly band about 4 cm in width. The border of this zone is comprised of dull red scaly papules. The latter extend around the sides of the wrist and over the dorsum and are irregularly scattered over the back of the hand. There are moderate dryness and scaling but little or no thickening. A general physical examination revealed ptosis of the left upper eyelid. The blood pressure is 150 systolic and 100 diastolic. A neurologic examination revealed normal conditions. There are no other noteworthy observations.

Biopsy of a specimen from the left wrist revealed only chronic inflammatory changes. The Hinton and Wassermann reactions of the blood were positive.

#### DISCUSSION

DR JACOB H. SWARTZ: The border is not nodular, although it is elevated. Has infection by *Trichophyton rubrum* been ruled out?

DR G. MARSHALL CRAWFORD: I do not think that possibility was discussed. The diagnosis was made clinically before the pathologic report was returned. When one looks at the section after the report of a positive serologic reaction, the interpretation is apt to be colored, but I could not have made a diagnosis of syphilis histologically. I should like to have Dr. Lever's opinion.

DR WALTER F. LEVER: The section did not suggest syphilis, because the vascular changes were not characteristic and there were few plasma cells. In most cases of secondary and early tertiary syphilis it is difficult to make a definite diagnosis on histologic grounds, and I believe that clinical means are more reliable.

#### A Case for Diagnosis (Dermatitis Medicamentosa?) Presented by Dr. JOHN ADAMS JR., Boston

S. B., a 67 year old white man of Italian descent, was admitted to the dermatologic ward of the Massachusetts General Hospital in February 1945. Six months previously, "blisters" had appeared on the left wrist, which were attributed to the leather strap of his wrist watch. The eruption became more pronounced and gradually spread to involve the whole body. A profusion of local applications had been used before the patient was admitted to the hospital, and some of these were felt to have been aggravating.

At the time of hospitalization there was a generalized dry, erythematous squamous dermatitis with extensive excoriation. Some areas were lichenified. There was moderate edema of the legs. A biopsy on admission revealed no diagnostic abnormality. Except for a white cell count of 10,000 and 27 per cent eosinophils in the differential smear, the results of the routine hematologic examination and the blood chemistry were within normal limits. The dermatitis became progressively worse, with the development of vesicles and bullae, especially on the legs. A pigmentary change began about this time and the entire skin has become steadily darker. A month after admission he contracted an acute pulmonary infection, which was treated with sulfadiazine. After this infection his renal function failed. On March 23 the nonprotein nitrogen content of the blood was 126 mg per hundred cubic centimeters. It has slowly dropped to 75 mg per hundred cubic centimeters at the last reading. There is albumin (4 plus) in the urine.

As seen today, this man presents a generalized pigmentation of dark brown, with a mottling of almost black pigment on the extremities. The legs, the volar

aspects of the wrists and the temples show numerous scars of 0.5 to 1 cm in diameter with complete depigmentation. This change is most pronounced on the ankles, where a few partially dried bullae are interspersed among the scars.

## DISCUSSION

DR JOHN G. DOWNING: My diagnosis is dermatitis medicamentosa, probably due to the sulfadiazine.

DR JACOB H. SWARTZ: I followed this patient while he was in the ward and before he was presented by Dr. Adams and I questioned whether or not the disease was a drug eruption. The blood sulfonamide level was determined ten days after sulfadiazine was administered, and the report was 2.6 mg per hundred cubic centimeters. I think that the eruption is dermatitis medicamentosa.

DR FRANCIS M. THURMON: When there is retention of one of the sulfonamide compounds over such a prolonged period, is there no way of elimination except by forcing fluids?

DR GEORGE E. MORRIS: That is the way to get rid of it.

DR CHARLES W. O'NEILL: I have a theory in regard to neutralizing sulfonamide compounds. The vitamins are destroyed by these compounds, by the same token, could they be destroyed with large doses of vitamins?

DR JACOB H. SWARTZ: Paraaminobenzoic acid is supposed to inactivate sulfonamide compounds. Why not try it on this patient?

DR GEORGE E. MORRIS: It should be pointed out that some of the vitamins interfere with the ability of the bacteria to react to the sulfonamide drugs. There is absolutely no chemical reaction between the vitamin and the sulfonamide derivative, thus, there can be no destruction, inactivation or increased secretion because of the intake of vitamins.

DR C. GUY LANE: It has been my opinion that the disease in this case is more consistent with lichen planus bullosa than with a drug eruption. It seems to me that when I first observed this man he had lesions on his arms which were certainly lichenoid in character. I do not remember that I saw any real striae, and the papules were not all exactly angular, but they fitted into the picture of lichen planus rather than into that of a drug eruption. Scratched papules in many instances can become lichenoid in character. The development of new bullae such as the large one seen today certainly should not occur unless the patient has had more of a sulfonamide compound, and he has had none. I do not know whether a later sulfonamide level has been obtained. Lichen planus of the bullous type is unusual, but it seems to me that this diagnosis fits this case better than a drug eruption, although I realize that the nonprotein nitrogen level could be explained by a reaction to a sulfonamide compound better than by lichen planus.

**A Case for Diagnosis (Dermatitis Herpetiformis or Pemphigus?)** Presented by DR. F. RONCHESI, Providence, R. I.

G. F., a 24 year old white woman, was presented with a generalized eruption of about a year's duration. The onset was marked by pruritic bullae which apparently arose from normal skin and ruptured soon after their appearance. There has been no improvement from the use of numerous forms of topical therapy. Sulfapyridine was given orally for many months, without notable effect, and the eruption has grown progressively worse.

Scattered practically all over the body are moderate numbers of thin-walled, impetigo-like bullae, 1 to 2 cm in diameter. They contain clear fluid, have no inflammatory halo and rupture with the slightest trauma. Many have been replaced by straw-colored crusts.

The results of the routine examination of the blood and the urine were within normal limits. The fluid contents of the bullae were sterile on culture. The result

of the phytopharmacologic test of Pels and Macht was reported as 59 per cent (normal 70 to 75 per cent) The Wassermann reaction of the blood was negative

## DISCUSSION

DR JACOB H SWARTZ I should like to suggest the Sencar-Usher syndrome for consideration The patient has lesions over the nose and a positive Nikolsky sign, which go with this syndrome

DR JOHN G DOWNING Darier mentioned a bullous eruption which is called *pemphigus hysterique*, occurring in young females (Darier, J *Presis de dermatologie*, Paris, Masson et Cie, 1923, p 222)

DR WALTER F LEVER I agree with the diagnosis of Sencar-Usher pemphigus The good general condition of the patient and the duration of her disease are not at variance with this diagnosis

## METROPOLITAN DERMATOLOGICAL SOCIETY

Royal M Montgomery, M D, President

James Lowry Miller, M D, Secretary

April 16, 1945

Dermatitis Venenata Presented by DR ROYAL M MONTGOMERY

E M, a white woman aged 46, has had a dermatitis of some part of her body for over ten years The eruption started on the palms ten years ago Two years ago, following roentgen therapy to the palms, the eruption spread to the arms, legs and feet When first seen, seven months ago, she had scattered papules on the neck and arms There was maceration on and between the toes

At present, there is dermatitis of the face, eyelids and neck There is mild dermatitis of the arms and hands, which she keeps covered with a paste of zinc oxide and starch The feet are free from maceration between the toes The Wassermann reaction of the blood was negative An examination revealed no tinea between the toes The result of a patch test with paraphenylenediamine (2 per cent) was negative

In June 1939, the results of patch tests made elsewhere with oil of orange, crude coal tar, Coty's perfume, Macy's shoe polish, Johnson's floor wax, Stafford's silver polish, powder and benzine were positive

## DISCUSSION

DR RICHARD J KELLY I favor the diagnosis of dermatitis venenata I think that the patient deserves a fair investigation, and I suggest that she get the most bland treatment at the present time

DR MAURICE J COSTELLO This patient has contact dermatitis with eczematous features I am sure that the dermatologists who have seen her have had trouble finding the cause of her eruption Some one might come on it accidentally rather than find it by the usual thoroughgoing methods The patient stated that when she goes away for the summer the eruption improves, only to recur after she returns

DR ROYAL M MONTGOMERY This patient presents a problem in that she neglects to carry out my suggestions for treatment She has been to different dermatologists while she has been under my care This causes confusion in her mind I believe that she should be hospitalized, use only the preparation prescribed and be given patch tests to find out the sensitizing agents

Giant Urticaria with Lymphedema Presented by DR LESLIE P BARKER

A B, aged 20, was first seen on March 22, 1945, at which time she gave a history of swelling of the nose, upper eyelids and cheeks for a period of two

years While she was away at school two years ago, she woke up one morning with her eyelids and nose tremendously swollen, without redness, pain or fever The acute part of the edema subsided within twenty-four hours, but since that time the swelling of the nose and, to a less extent, of the eyelids has never entirely subsided She has had rather frequent attacks of the acute swelling during the two years She is certain that any foods containing wheat products cause an attack Otherwise, she has no idea of any etiologic factor

She has had hay fever since childhood Her father also has had hay fever One grandmother had asthma Her hay fever has been produced by dust and air-borne pollens An examination and roentgenograms of the sinuses showed no involvement

There is a firm, rubbery edema of the entire nose, especially over the bridge, and a moderate amount of edema of the eyelids There is neither discoloration of the skin nor sign of inflammation A recent thorough study by an allergist, which included tests with foods, air-borne pollens, fungi, and bacteria cultured from the nose, nasopharynx and throat, showed the following positive results Strongly positive reactions were obtained from grasses, especially ragweed, and also dust and feathers Moderately positive intradermal reactions were given to *Streptococcus viridans* obtained from the nose and throat The results of intradermal scratch tests and patch tests with wheat were all negative

#### DISCUSSION

DR MAURICE J COSTELLO From time to time at the dermatologic societies similar cases have been presented in which there has been involvement of the eyes, nose, cheeks and lips, and less frequently of the ears and genital region The best results in my experience and in the experience of others have been obtained from the administration of sulfonamide drugs, especially sulfapyridine, which is the most effective of the sulfonamide compounds One would risk less by giving the patient a trial treatment with penicillin, 25,000 units being administered every three hours for two weeks and possibly longer

DR J LOWRY MILLER I believe that by now chronic lymphangitis is present For this reason a trial treatment with penicillin is indicated, as the results in some cases have been excellent Larger doses of penicillin over a shorter time are to be preferred to smaller doses over a longer time

DR THOMAS N GRAHAM I agree with Dr Miller that it is advisable to start with larger doses and to discontinue the use of medicament after three or four days if there is no improvement

DR W SODA (by invitation) I have treated a number of patients with penicillin for a period of one to two weeks In my experience at Bellevue Hospital one or two weeks is required for definite improvement to be noticeable

DR RICHARD J KELLY I agree entirely with Dr Costello—that is, sulfonamide compounds or penicillin should be used, but in concentrated doses I think that the woman has lymphangitis of the erysipelatous type

DR ROYAL M MONTGOMERY This condition should be diagnosed as lymphedema I am in agreement with the opinions of the other men about sulfonamide drugs and penicillin I think that it should be pointed out, as Dr Soda has said, that the results occur not in a few days but in a few weeks with the medicaments mentioned

DR LESLIE P BARKER The history that the eruption subsides slightly but never completely makes me feel that, although she may have had giant urticaria initially, there is a great deal of chronic lymphedema present at this time that may be permanent

The case has been presented for suggestions as to treatment I wonder if any one has had experience with radiotherapy in these cases One patient at Vanderbilt Clinic with lymphedema of the upper lip improved with sulfonamide drugs and

filtered roentgen ray therapy I have hesitated to give radiotherapy in this case because of the possible danger to the visual nerve (optic nerve)

**A Case for Diagnosis (Bowen's Disease? Tuberculosis Cutis?) Presented by DR THOMAS N GRAHAM**

W R, a white man aged 42, was first seen by me on March 7, 1945. He complained of an eruption of approximately twenty years' duration on the left hand. He stated that the eruption had started as a small raised patch, which gradually spread peripherally to its present size. He was treated a year ago with fractional roentgen ray therapy, with no improvement. His occupation for the past two years has been clerical, and previously his work consisted of handling raw meat. There has been no pruritus.

An examination showed an irregular erythematous scaly patch 4 by 5 cm in diameter. The margin is moderately indurated. In the center of the patch is a verrucous area. There is some superimposed crusting on the remainder of the patch. Adjacent to the verrucous area there is a scar, the site of a lesion which was removed with a cautery a number of years ago.

A biopsy specimen showed the epidermis to be acanthotic, with a nonparakeratotic scale and with well defined rete pegs. Many of the prickle cells contained large and hyperchromatic nuclei as well as mitotic figures. There was a zone of inflammatory exudate in the corium. The histologic picture was consistent with but not definitely diagnostic of Bowen's disease.

#### DISCUSSION

DR J LOWRY MILLER I believe that the man has keratoses of the palm and the soles which are characteristic of those caused by arsenic. The lesion on the back of the hand is a Bowen type of epithelioma, which has been seen frequently arising in patients who have taken arsenic over a long period.

DR LESLIE P BARKER In view of the pluglike keratoses of the palm and the soles, I think that this patient definitely has arsenical keratoses. The irregular erythematous scaly patch on the hand I think is Bowen's type of precancerous lesion. The blood should be tested for the presence of arsenic, and if there is no arsenic the patient should have several doses of sodium thiosulfate and a test of the blood for arsenic should be repeated. A biopsy of tissue from the lesions of the hand should be performed.

DR RICHARD J KELLY I agree with the previous speakers. I think that the patient definitely has arsenical keratoses. I am in disagreement with desiccation as a method of treatment. I think that the patient should be given thorough fractional roentgen ray therapy by the Coutard method. The lesion probably would entirely disappear with this type of therapy. I agree with Dr Barker that the patient should be tested for the presence of arsenic.

DR MAURICE J COSTELLO I agree with the diagnosis of arsenical keratoses. The lesions are typical. The point that Dr Fox made about arsenical keratoses is that the lesions are often on the sides of the hands and the sides of the fingers. The large lesion could easily be mistaken for tuberculosis verrucosa cutis. I am under the impression that the lesion would not respond to roentgen rays. I think that it would be simple to inject a solution of procaine hydrochloride into the lesion and destroy it by surgical diathermy.

DR ROYAL M MONTGOMERY I believe that this man has Bowen's disease superimposed on or caused by arsenical keratoses. A similar case was presented by me before this society four years ago (*ARCH DERMAT & SYPH* 45:407 [Feb] 1942). I have encountered a half dozen other cases since then. Desiccation and curettage of lesions of the Bowen type are the best method of treatment. Arsenical keratoses are difficult to cure.

DR THOMAS N GRAHAM I agree that this is probably a case of Bowen's disease superimposed on arsenical keratoses.

Hydroa Vacciniforme (Hydroa Aestivale) Presented by DR J LOWRY MILLER

F S, a girl aged 14, was first seen at Vanderbilt Clinic in September 1944. She complained of red vesicular lesions which have appeared on the hands since she was 1 month of age after even slight exposure to sunlight. In the winter no lesions have been present. In the summer, during the hot weather she perspires little, but she has never collapsed from the heat. The mother has noticed that she does not perspire as do the other members of the family. The patient has been free of all lesions during this past winter. Two weeks ago, a few lesions again appeared on the face.

An examination showed a few pea-sized red scaling areas at the sites of dried-up vesicles. These lesions are present on the nose and cheeks. A complete blood cell count showed normal conditions. The blood cholesterol level was 179 mg per hundred cubic centimeters. The basal metabolic rate was +10 per cent.

Treatment has consisted of injections of solution of liver intramuscularly and administration of vitamin B complex by mouth.

DISCUSSION

DR THOMAS N GRAHAM: Patients with hydroa vacciniforme present definite scarring from previous lesions, but I did not see scarring in this patient. One of the diagnostic features is scarring from previous lesions, with the appearance of bullae and vesicles during the summer when the areas are exposed to the sun. I am unable to suggest a diagnosis in this case.

DR W SODA (by invitation): I think as Dr Graham does. The patient has a history of recurring lesions. On inspection there did not seem to be evidence of much scarring.

DR RICHARD J KELLY: I suggest that she has dermatitis herpetiformis in one form or another which could be interpreted as hydroa vacciniforme. I prefer the diagnosis of dermatitis herpetiformis.

DR MAURICE J COSTELLO: As Dr Graham mentioned, I do not see the rather conspicuous scarring that should follow or be part of the picture of hydroa vacciniforme. One had to look closely for a few areas of depigmentation and superficial scarring. I think it is barely possible that this patient has had prurigo hiemalis appearing on the extensor surfaces of the extremities. I suggest that the child be exposed to sunlight for increasing periods and be given an ointment which would make the skin somewhat impervious to sunlight.

DR LESLIE P BARKER: The location of this eruption on the cheeks and the arms, consisting of a few pea-sized crusted areas, suggests hydroa vacciniforme, but the lack of scarring is certainly against that diagnosis.

DR J LOWRY MILLER: I saw the patient last fall, at which time there were bullous lesions involving the arms and the face limited to the areas exposed to sunlight. Similar lesions have been present since the patient was 1 month of age, appearing each spring and clearing in the early fall. I believe that there is no question that this is a case of sensitivity to light, a mild hydroa vacciniforme. The child was underweight and run down. She was given injections of liver substance. She gained weight and appears physically much better. No lesions have been present all winter. With the approach of spring, the lesions began to appear on the nose, which is the first location involved each year. The child has been given ultraviolet irradiation but is not able to build up sufficient resistance to prevent lesions on exposure to sunlight. The mother is an intelligent woman, and I believe that she is forced to keep the child out of the sun.

NOTE—Sections of cutaneous tissue disclosed a moderate hyperkeratosis and a slight acanthosis, with individual epithelial cells being hydropic. The cutis appeared to be somewhat edematous, with slightly dilated capillaries and minimal perivascular infiltration.

**Syringocystadenoma** Presented by DR J LOWRY MILLER

M M, a Puerto Rican aged 23, was admitted to the New York City Hospital clinic on April 9, 1945, complaining of lesions of the eyelids and the "V" of the neck which have been present for the past five years. She has never had any treatment.

An examination showed about a dozen discrete pinhead-sized to split pea-sized round, smooth nodules which are somewhat brownish to yellow. Similar lesions are situated on the "V" of the neck. No laboratory reports have been received as yet.

**DISCUSSION**

DR W SODA (by invitation) The small round sharply defined lesions seemed to fit definitely with my concept of a disease involving the sudoriferous glands. I agree with the diagnosis of syringocystadenoma.

DR LESLIE P BARKER I agree with the diagnosis of syringocystadenoma. Patients with this disease are resistant to treatment, and I should like to know whether any of the physicians have had any experience with light electrodesiccation. I have tried it in several cases, but there is some scarring produced and the lesions are not eliminated, also, new lesions continue to appear.

DR RICHARD J KELLY I agree with the diagnosis. As far as Dr Barker's question is concerned, I do not think that roentgen rays would help.

DR MAURICE J COSTELLO The patient has multiple benign cystic epitheliomas. My idea of syringocystadenoma is that it is a disease which is confined to the chest, back and abdomen. I have never seen it on the face. If treatment is necessary and the lesions prove to be multiple benign cystic epitheliomas, I have treated them successfully with electric cautery.

I suggest that you perform a biopsy on specimens from two places, one from the eyelids and the other from the chest.

DR J LOWRY MILLER Biopsy would of course have to be performed to determine the diagnosis between multiple benign cyst and syringocystadenoma.

NOTE—Biopsy sections taken from both the neck and the eyelid were diagnosed as syringocystadenoma.

**A Case for Diagnosis** Presented by DR MAURICE J COSTELLO and Dr W SODA

J O, a 54 year old Polish man, was admitted to Bellevue Hospital on March 20, 1945. About fifteen months previously, purpuric lesions had developed on both feet and legs. Since then these lesions have had a tendency to recur, in the afternoon especially. About ten months ago, he noticed several small growths on both ankles. These continued to increase gradually in size. He noticed no pain or particular discomfort. Two months later lesions of the same type developed on both knees. Since he has had these growths, the purpuric lesions have been more prominent. His past history revealed that a nasal polypectomy had been performed.

Multiple discrete, small, erythematous, macular lesions are present on the legs and the dorsa of the feet. There are also multiple, pale pink, sharply circumscribed, smooth-topped nodules, the size of hazelnuts and even larger, involving the lateral aspect of the left ankle and the calcaneal area of both ankles and also the anterior surface of both knees. Along the lateral border of the right foot are seen and felt two firm, diffuse, slightly elevated nodules. On the thenar eminence of the left palm is also seen a circular, smooth, diffuse, elevated nodule with a depressed center. There are varicosities of both legs with brownish pigmentation. The patient has bilateral chronic dacrocystitis, bilateral cervical adenopathy, partial occlusion of the nasal vestibules and two nodular prominences at the head of the left radius. The urine was normal. The blood was essentially normal except for mild leukocytosis. The Wassermann reaction was negative. The blood cholesterol level was 182 mg per hundred cubic centimeters and that of cholesterol esters 100 mg per hundred cubic centimeters. Tuberculin in a 1:100,000 dilution elicited



of a split pea to that of a large bean. In addition, there is a bilateral tenosynovitis of the wrists, which superficially appears like a simple ganglion. Generalized adenopathy is present.

Tuberculin in a dilution of 1:100 elicited a positive reaction. A roentgenogram showed a fine nodulation throughout both lungs, with some hilar enlargement bilaterally, a widening of the superior mediastinum, which was probably due to paratracheal lymphadenopathy, and multiple thin-walled giant bullae in the right lung. The impression was that of sarcoidosis with bullous emphysema. Roentgenologic studies of the bones of the hands revealed small cystlike formations at several phalanges and similar lesions in several carpal bones, due to sarcoid infiltration. A histologic section was diagnosed as sarcoid.

#### DISCUSSION

DR E. ALMORE GAUVAIN: I agree with the diagnosis. The value of a test with tuberculin in a 1:100 dilution is practically nil, since some degree of reaction can be obtained in almost any one with this concentration. One should use about a 1:100,000 dilution.

DR JOEL SCHWIFIG: I want to ask Dr Pensky whether therapy has as yet been instituted. I believe that one is dealing with a special type of sarcoidosis in this case, as is seen in the American Negro and described by Klauder and Weidman. The clinical manifestations are characteristic—cherry-sized nodules are scattered over the trunk and the face. Klauder and Weidman believe that such eruptions are a sarcoid-like manifestation of tuberculosis of the skin. They find a positive tuberculin reaction as a rule. I suggest, therefore, further study with that in mind and also a determination of the albumin-globulin ratio in the blood, which is pathognomonic.

DR NATHAN PENSKY: There is sufficient evidence to rule out the diagnosis of leprosy. The peculiar and characteristic involvement of the lungs, hands, skin and lymphatic glands is that found in sarcoidosis and not in leprosy. Tubercle bacilli have never been found in the sputum or by gastric extraction.

Up to the present time no therapy of definite value has been discovered. In some cases the cutaneous lesions resolve spontaneously, in others, progression continues in spite of treatment. A considerable number of patients suffering with this disease contract, and die from, generalized tuberculosis. The possibility should be borne in mind that these persons, having been hospitalized at an institution for patients with tuberculosis at some time during their life, may have contracted tuberculosis. One must remember that roentgenograms of the pulmonary fields resemble extensive tuberculosis and that often hospitalization as well as prolonged study is necessary to rule out tuberculosis.

There are several important points concerning sarcoidosis that should be stressed. Only one third of the patients with this disease present cutaneous lesions. About half the patients with progressive tuberculosis eventually die of the disease. Some competent investigators have found that in animals inoculated with tissue obtained from patients who have sarcoidosis tuberculosis develops on one or two passages. The association of this disease with the involvement of the reticulo-endothelial system as well as the termination of many of these cases due to tuberculosis is more than coincidental.

**Tinea Barbae** Presented by DR SEYMOUR H. SILVERS

I. B., a butcher aged 39, consulted me for boils of three weeks' duration on the face. He works exclusively at skinning calves, and he often brushes his face against the fur of the animals.

When he was first seen, four weeks ago, he had a hard, indurated red mass, the size of a small tangerine, peppered with pinhead white pustules, on the left side of the neck under the chin. Two smaller but similar masses, each the size of a large marble, were present on the right and left sides of the distal parts of the chin.

At present, the lesions on the chin are flat, red and devoid of hair. The lesion on the neck is red and indurated, with a few elevated papules. There are few hairs left in this area.

Repeated cultures of material from the infected areas did not produce a growth, and therefore the organism could not be identified.

#### DISCUSSION

DR ABRAHAM WALZER. It is generally difficult to isolate the fungus. As a rule the eruptions respond to roentgen ray treatment.

DR JACOB SKEER. Cases like this one are, to my mind, extremely uncommon. I saw 1 patient, an adult, with such an eruption in the bearded region. The lesions



Tinea barbae

were somewhat smaller than those in the present cases, but more profuse, involving the chin, the lower jaw and the neck.

DR SEYMOUR H. SILVERS. I have not seen a patient with tinea barbae for many years. This eruption is typical, and the diagnosis has been confirmed by direct examination of the hair. The patient skins approximately fifty calves a day and thus has ample opportunity to become infected. He has improved greatly within four weeks. He is receiving roentgen ray treatment, injections of trichophytin and manual epilation.

#### Prurigo Nodularis Presented by DR ABRAHAM WALZER

R. W., a Negro aged 29, single, an ammunition handler by occupation, was first seen in the dermatologic clinic of the Jewish Hospital of Brooklyn two weeks ago. He gave a history of syphilis of a number of years' duration, and he had been treated at the Board of Health Clinic for the past four months. He had received about six intravenous and six intramuscular injections. The cutaneous

lesions for which he sought relief at this clinic had appeared two months ago, while he was receiving these injections. The Wassermann reaction of the blood was positive.

At present he shows lesions limited to the hands, fingers, forearms and backs of the elbows. These consist of many scattered, pea-sized or larger, raised, hard, smooth nodules. These are pruritic, as is evidenced by the scratched-off tops. Some of these are covered with thin scales or scabs, which on removal show a number of tiny, pinpoint openings.

#### DISCUSSION

DR JACOB SKEER. The lesion appears to be a discrete nodule, about the size of a pea or smaller, with a superficial crust. Removal of the crust shows a little indentation, which may be necrosis or ulceration, this is not compatible with prurigo nodularis. These lesions are firm rounded nodules with a fine scale, which are intensely pruritic. They occur more on the lower than on the upper extremities, but they do occur on all the extremities and may occur on the face too. The lesions seen tonight suggested to me some type of papular necrotic tuberculid.

DR JOEL SCHWEIG. I agree with Dr Skeer. To my mind this is definitely not a case of prurigo nodularis. The location is not typical. The lesions do not present the characteristic nodular tumors, which would cause much more discomfort than the patient has. I believe that one is dealing in this case with keratoderma circumscriptum, possibly acquired in the course of the patient's work in a machine plant (not his regular occupation), and may belong in the group of industrial dermatoses.

DR ABRAHAM WALZER. Prurigo nodularis usually occurs on the forearms, arms, thighs and legs, and also on the hands. The lesions in this case developed in the midst of syphilitic treatment and are therefore not likely to be those of syphilis. They appear to be a little too hard to be sarcoid. They are apparently too large for a papulonecrotic tuberculid. Therefore, to my mind, the only diagnosis that is possible is prurigo nodularis. The histologic studies may clear up the diagnosis.

#### Pseudopelade. Presented by DR ABRAHAM WALZER

K. C., a girl aged 14, was first seen at the dermatologic clinic of the Jewish Hospital of Brooklyn a few days ago. She gave a history of a bilateral mastoidectomy at the age of 8 years.

The present disease began about two years ago. The hair on the side of the head fell out suddenly and has never grown back. Examinations of the blood and the urine showed nothing abnormal. The Wassermann reaction of the blood was negative.

As presented, she shows an elongated area of alopecia, apparently composed of three joined, dime-sized patches. The central part is depressed, atrophic and faintly erythematous. The edge presents irregular indentations of tufts of hair.

#### DISCUSSION

DR MORRIS M. ESTRIN. I think that this is a case of self-inflicted injury. Both the girl and her mother intimate that this is so. The girl said that she does not twirl her hair, but that sometimes she will pull at it and that she also rubs that area continuously. There is no atrophy to be seen, and I think that the patient's action is in keeping with trichotillomania.

DR E. ALMORE GAUVAIN. I agree with Dr Estrin.

DR JACOB SKEER. The only thing against the diagnosis of trichotillomania is that the lesion is too well defined. I do not believe that that is the correct diagnosis, therefore. I also feel that there is a tendency to atrophy, and I agree with the diagnosis as presented.

DR ABRAHAM WALZER. If these lesions were induced, the edge would not be so sharply demarcated. The floor would not be smooth and atrophic.

NEW YORK ACADEMY OF MEDICINE, SECTION OF  
DERMATOLOGY AND SYPHILISHarry C Saunders, M D , *Chairman*Frank Vero, M D , *Secretary*

May 1, 1945

Generalized Vitiligo Alopecia of Undetermined Cause Presented by  
DR HELEN CURTH

A R, a Negro woman aged 40, is presented from the Vanderbilt Clinic with a generalized cutaneous disease of fourteen years' duration and alopecia of two months' duration. The patient was born with rather a dark skin, which remained that way until she was 26 years old. At that time her skin gradually began to turn white, first on the arms, trunk and legs and finally on the face. The entire skin stayed white with the exception of that of the scalp. Itching of the scalp and loss of hair started a couple of months ago. After the cutaneous lesions had begun she received subcutaneous injections in the arms, given her by a private physician. The patient said that she had no "bad blood" or infections. Her skin began to turn dark again about four months ago.

At present, the patient's skin is for the most part white. She has symmetric islands of pigmented skin on her nose, cheeks, lips, chin, palms, soles and fingers. On the arms are seen small plaques of pigment. There are patches of alopecia on the frontal areas of the scalp, which otherwise appears normal. The hair is dark, with the exception of that on the sides, which is white.

A determination of arsenic in the blood is pending.

## DISCUSSION

DR CHARLES S MILLER This woman has never been a patient of mine, but I have seen her about town for the past fourteen years and have not observed any change.

## Basal Cell Epithelioma of the Forearm Presented by DR JACK WOLF

J M, a man aged 64, was admitted to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital with a large lesion of five years' duration on the middle third of the right forearm. The lesion is irregularly rounded and sharply circumscribed and is about 3 inches (7.5 cm) in diameter. The central area, of approximately the size of a 25 cent piece, is whitish, smooth and atrophic and surrounded by an erythematous, profusely crusted zone about  $\frac{1}{2}$  to  $\frac{3}{4}$  inch (1.2 to 1.9 cm) in width. At the periphery there is a fine, sinuous, raised, cordlike border.

A biopsy section from the peripheral zone confirmed the clinical diagnosis of basal cell epithelioma.

## DISCUSSION

DR CHARLES WOLF In that location one would expect a squamous cell epithelioma or a prickle cell epithelioma.

DR MAX SCHEER When I first saw the patient, I thought that the lesion would probably be Bowen's disease, and I was surprised when the histologic report showed a pure basal cell epithelioma. Usually in these crusted lesions one expects to find a prickle cell epithelioma. In any event, according to my experience, basal cell epithelioma is rare on the extremities.

DR EUGENE F TRAUB The center of a lesion of this type frequently heals as the active border spreads peripherally. In this case, the central scar was probably changed by factors other than treatment. Squamous cell lesions are encountered on the extremities much more frequently than are basal cell lesions, but I believe that the appearance in this case is suggestive not so much of a

squamous cell epithelioma as that of Bowen's disease, for which this lesion could have been mistaken

DR JACK WOLF This is an excellent example of the banal basal cell epithelioma encountered so frequently on the extremities

#### Multiple Keloids in Twin Sisters Presented by DR DAVID BLOOM

E M G, a Negro woman aged 26, registered at the clinic of the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on April 25, 1945, complaining of numerous cutaneous tumors of ten years' duration

On the left and right arms, the right shoulder and the left knee there are firm tumors from the size of a walnut to that of an orange. On the sternum and both breasts there are elongated, raised firm plaques with clawlike lateral projections. Some of the lesions have been treated with roentgen rays and radium, and they present signs of radiodermatitis.

The first lesion to appear was that on the left arm, following vaccination for smallpox.

An apparently identical twin sister has similar multiple keloids, which also began after vaccination.

The case is presented because of the unusually large multiple keloids, because of the appearance in probably identical twins and for suggestions as to therapy.

#### DISCUSSION

DR FRED WISE It is generally known that treatment is useless in cases of this kind, and all one can say is that it is a tragedy for a person to have keloids of this extent and size. Excision is followed by more keloids, sometimes larger than the original ones, and radiation therapy is of no avail for lesions of this size and thickness.

DR EUGENE F. TRAUB Dr. Wise has covered the main points, and I just wish to touch on those on which there could be a possible difference of opinion. Several of the largest lesions, even though located on the back, where the procedure might be painful, might possibly be excised and the area promptly irradiated. The irradiation should follow immediately after the removal of the lesion and be continued in sufficiently large dosage to prevent a regrowth, even though mild sequelae of irradiation might result from such extensive therapy. It would be impossible to get much of a result by irradiation in a case of this type, in my opinion, without some sequelae.

DR DAVID BLOOM I shall follow the advice of Dr. Traub and treat the keloids surgically, followed by roentgen irradiation. In looking over the literature in regard to keloids in several members of the same family, I found four references, one by Hutchinson, in 1879, who reported such lesions in three generations of a family, and one by Kaposi, in three sisters. The statement of the patient that the first keloid appeared in each twin soon after vaccination seems to me of interest.

#### A Case for Diagnosis (Lupus Erythematosus? Chloasma?) Presented by DR JACK WOLF

V C, a woman aged 23, was admitted to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, with an eruption of three years' duration on the cheeks.

The eruption first manifested itself in the form of red spots, following a sunburn. These became brown and increased in size.

There is a butterfly-shaped lesion on the cheeks and extending across the nose, consisting of deeply pigmented macular lesions covered with fine adherent scales.

According to a biopsy section from this area the disease was reported as lupus erythematosus.

#### DISCUSSION

DR ISADORE ROSEN I am not inclined to agree with the diagnosis as presented, for there are no clinical features which would fit in with lupus erythematosus. All

that is present is a symmetric pigmentation on both cheeks, which in all probability is due to some cosmetic the patient has applied

DR DAVID BLOOM I agree with Dr Rosen that a diagnosis of lupus erythematosus should not be made in this case merely because of the butterfly configuration. I believe that this hyperpigmentation has followed some dermatitis. As to the occurrence of pigmentation in lupus erythematosus, I have observed a number of cases in which pigmentation was pronounced, and I believe that this association is not rare.

DR EUGENE F. TRAUB In this case it is difficult to arrive at a clinical diagnosis, because the findings are not clearcut. There appears to be some inflammatory reaction and scaling and some slight pigmentation. How much of the pigmentation may be due to the naturally dark type of skin of the patient is difficult to surmise. For these reasons, I do not believe that this is a case of chloasma, as one does not ordinarily see inflammation and scaling as part of this process. Contact dermatitis could not be excluded, nor can the diagnosis of lupus erythematosus. It would appear to me to be necessary for Dr Wolf to exclude entirely all possible contact irritations before a diagnosis of lupus erythematosus could be established.

DR MAX SCHEER When the patient first presented herself at the clinic, the diagnosis favored was chloasma. A biopsy specimen showed the picture of lupus erythematosus. The pigmentation may be due to the color of the patient, who is a Puerto Rican and has the type of skin that tends to pigment.

DR FRED WISE After what Dr Scheer has just said, it would be presumptuous to say that the patient's eruption is not lupus erythematosus, and yet I am greatly prejudiced against that diagnosis. It is a well known fact that the poorer class of Latin Americans uses cosmetics of inferior grades, which often contain mercury. An entire volume has been written on this subject by an Argentine dermatologist. He explained that in nearly every one of these cases the cause of the pigmentation is some form of cosmetics or the persistent use of them rather than the cosmetic itself. The history given me by the patient is that she had no redness at all preceding this eruption. She said that there was little pigment, but she gave no history of eruption that would make one think of lupus erythematosus. In spite of all that has been said, I still believe that, if she did have lupus erythematosus and was cured, all she now has is pigment from cosmetics. Maybe the cosmetics were used to conceal the lupus erythematosus, but I should certainly not make a diagnosis of lupus erythematosus on present appearances.

DR JACK WOLF There are many controversial features in this case and many factors that tend to favor the diagnosis of lupus erythematosus, namely, scaling, some erythema and the history, which, as the patient gave it to me, was that a few red spots developed following a sunburn. A positive clinical diagnosis of lupus erythematosus was not made, but that possibility was entertained on account of the distribution and the history. Much to my surprise, the histologic diagnosis confirmed the probability of lupus erythematosus. Chloasma, cosmetic dermatitis and dermatitis venenata will not give the histologic picture of lupus erythematosus, so there is at least reasonable ground for entertaining that diagnosis.

#### LOS ANGELES DERMATOLOGICAL SOCIETY

A Fletcher Hall, M D, *Chairman*

Clement E Counter, M D, *Secretary*

*April 10, 1945*

**Necrobiosis Lipoidica Diabeticorum** Presented by DR HAL E. FREEMAN.

M D B is a woman aged 36 years. She has had diabetes mellitus for eight years. The present lesions on the right leg and foot have existed for five years.

Three lesions are present. One is on the anterior surface of the right leg halfway between the knee and the ankle. It is slightly raised, with telangiectasia and a yellowish red color. It is oval, about 4 by 7 cm in its diameters, and in the upper middle portion of this lesion is a healed ulcer about 2 cm in diameter. Another lesion is on the dorsum of the left foot. It is a smaller but not ulcerated tumor, and it is located in an old traumatic scar. A third lesion is on the left shoulder. It is a smaller and less highly colored tumor.

The blood cholesterol level has been as high as 334 mg per hundred cubic centimeters, and the blood sugar level has been 350 mg per hundred cubic centimeters. This was about one year ago. This patient is especially presented again after six months to show the benefit the Aloe vera leaf dressing has been in the healing of the ulcer.

#### Necrobiosis Lipoidica Diabeticorum Presented by MAJOR S B MAY (by invitation)

E W is a woman aged 22 who has moderately severe diabetes, which has been poorly controlled. Her present illness began three years ago, when a red patch appeared on the upper anterior surface of the right leg. This spot has persisted and gradually enlarged. There are no symptoms. It has never ulcerated.

The patient is a thin, undernourished, pale woman. On the upper anterior part of the right leg on the crest of the tibia are three more or less disconnected oval patches, which are defined. These areas are flat and slightly depressed and have a pale mottled appearance. The centers tend to be yellow with pink to red margins. Central scarring and fine scaling are present. The skin is mildly thickened and indurated. The lesions are not tender.

The blood sugar content has fluctuated from 47 to 532 mg per hundred cubic centimeters. The blood cholesterol level was 350 mg per hundred cubic centimeters.

A recent biopsy specimen showed an area of necrosis in the dermis, which was bordered in most places by narrow zones of large mononucleated cells having pale or fine foamy cytoplasm. The surrounding dermis showed infiltration by round cells and focal areas of lymphocytes. There was moderate flattening of the epidermal pegs. Near the base of the specimen there was an artery which showed muscular thickening of its walls. The epithelium was not changed. Stains for fat showed areas of fat extending into the dermis. There were a few scattered cells containing small deposits of fat. The treatment has included careful diabetic management for five weeks in the hospital. Improvement has been shown by the lesions becoming less defined and not so deeply colored.

#### DISCUSSION OF THE PRECEDING TWO CASES

DR WILLIAM MULVEHILL. Both these cases are instances of necrobiosis lipoidica diabeticorum. They are not exactly typical clinically, because of the large amount of infiltration in both of them and the color. Dr Freeman's patient did not have the yellow appearance that a patient with necrobiosis lipoidica diabeticorum should show. Both patients have had high blood cholesterol levels. In the cases of necrosis that I have seen, the higher the cholesterol level in the blood the more prominent was the cutaneous lesion. I believe that the infiltration and the color in both lesions are due to the high cholesterol content of the blood.

DR NELSON PAUL ANDERSON. I was interested some time ago in seeing an article by Dr John Harris, of New York, written before Dr Urbach described necrobiosis lipoidica diabeticorum. Dr Harris undoubtedly has described necrobiosis lipoidica diabeticorum under the title of Xanthoma Diabeticorum, An Unusual Process of Involution (Goldstein, E, and Harris, J. *Am J M Sc* **173**: 195 [Feb] 1927). It goes to show that cases of this disease were seen before Urbach called attention to them, but physicians called the disease by different names.

DR HAL E FREEMAN. Most dermatologists do not expect to find foam cells in the biopsy specimen from a case of necrobiosis lipoidica diabeticorum. If they

do see them, they think of xanthoma diabeticorum. In the last few months some one has written a long article in the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY on what he calls necrobiosis lipoidica diabeticorum with foam cells, and I did not see foam cells in the section from Major May's case. If I had found them, then I should have said that it was xanthoma diabeticorum, but I did not see them, so I think that his case is also a case of necrobiosis, as presented.

DR J WALTER WILSON. The Wuecher type of atrophy shown in the slide belongs to necrobiosis lipoidica diabeticorum and not to xanthoma diabeticorum.

MAJOR S B MAY (by invitation). There are two minor points that led me to question the diagnosis a bit. One was the asymmetry of the lesions. The lesions are solely on the right leg. The other was the improvement that the patient showed during a five week period in the hospital, where her only treatment was diabetic management. The lesions are now less prominent than before, with less erythema in the borders.

**Leukoderma Acquisitum Centrifugum** Presented by DR SAMUEL AYRES JR

G H, a boy aged 14, has had a number of moles scattered over the body for many years. Two of these lesions have undergone a progressive depigmentation in the past year. The lesion on the right side of the upper part of the back was originally dark, but during the past year the lesion became slightly more inflamed and more swollen and has gradually lost pigment, until now only a small central area is pigmented. The lesion on the right temple has similarly undergone a gradual loss of pigment during the past year.

There are a large number of brown moles ranging in size from that of a split pea to nearly that of a dime, which are flat and slightly elevated. These are scattered over the trunk, arms, neck and face. On the right side of the upper part of the back is a red brownish, slightly elevated mole the size of a split pea surrounded by a wide depigmented zone. Higher on the back is an oval, slightly thickened brownish mole half the size of a dime, within which are several irregular almost black streaks. At the lower right border of this mole is a small depigmented area. On the right temple within the hair line is a half dime-sized oval area with a pea-sized brownish slightly pigmented portion and a broad zone of depigmentation including white hair surrounding it.

#### DISCUSSION

DR KENNETH STOUT. One wonders about the mechanism in which pigment is formed in one part with a reduced amount of pigment in other parts.

DR M E OBERMAYER. I should like to call Dr Ayres's attention to the presence of a hyperpigmented macular lesion in the neighborhood of the leukoderma, that lesion is a lentigo and should be investigated for the possibility of early melanomatous changes.

DR SAMUEL AYRES. One ordinarily does not get a chronologic picture of how these lesions develop. According to the mother, these lesions were at one time all pigmented moles. Then apparently the one most pronounced on the back became somewhat inflamed, and then it began to lose pigment except in the center. The other moles have gone through a similar process. They all began as moles and then became inflammatory, then the pigmentation disappeared peripherally, leaving a central brown spot. The center is more erythematous than it is pigmented.

**A Case for Diagnosis (Parapsoriasis with Pigmentation, Urticaria Pigmentosa?)** Presented by DR MAXIMILIAN E OBERMAYER

On N F, a woman aged 26, three months ago an eruption appeared at the sides of her neck and within two weeks spread to cover the areas as seen today.

There is a generalized papulosquamous eruption which covers the body from the neck down to the soles, and it consists of closely set small papules. Some of these are prominent, erythematous and slightly infiltrated and show fine scaling.

The majority are maculopapular and hyperpigmented. No "whealing" can be elicited by friction.

The lesion removed for biopsy from the medial surface of the right thigh was one of the scaling papules. The section showed an epidermis with considerable hyperkeratosis and parakeratosis. There was slight follicular plugging as well as a mild degree of spongiosis in the prickle cell layer. The dermis was edematous and filled with a massive cellular infiltrate, which blended with a basal cell layer of the epidermis and was arranged perivascularly in the upper and middle layers. The infiltrate consisted mainly of lymphocytes. There were some plasma cells and only a few larger cells with massive nuclei.

#### DISCUSSION

DR W. H. GOECKERMAN: Most of the members debated in their minds a number of diagnoses, and urticaria pigmentosa possibly came into consideration as well as pityriasis lichenoides chronica. I first thought that it was the latter, then, on looking closer, I saw that the entire body was involved. I asked the patient how long it had been present, and she said three or four months. I see no reason why one should doubt her statement. Despite the unusual characteristics, I think that it is pityriasis lichenoides chronica.

DR ANKER K. JENSEN: One should not overlook the possibility of a drug eruption. She told me that she had taken Midol (a proprietary mixture containing approximately 0.462 Gm of acetylsalicylic acid, 0.016 Gm of einnamyl ephedrine and 0.052 Gm of caffeine) for a number of years for some menstrual disturbance. The appearance, distribution and onset are consistent with a drug eruption.

DR M. E. OBERMAYER: Though I presented the case purposely under two possible diagnoses so as not to bias your judgment, there was not a doubt in my mind that the disease is a nonvariiform variety of Haberman's pityriasis lichenoides et varioliformis acuta, with an unusual degree of postinflammatory pigmentation. There were a number of factors which aided in ruling out the possibility of urticaria pigmentosa, such as the clinical course of the individual lesions, which pass from an acute erythematous to a scaling stage and finally flatten out to leave hyperpigmented macules, the absence of "whealing" on friction and of mast cells in the section, and the age of onset. I appreciate Dr. Jensen's suggestion of a drug eruption, though I do not think that his assumption is correct, it has taught me to be more insistent in taking a history of medication.

#### Perforating Ulcer of the Foot in Two Sisters Presented by DR SAMUEL AYRES, JR.

The family history of V. E., a woman 27 years of age, shows that a sister has had pulmonary tuberculosis, a brother has diabetes and another sister has a lesion of the same type as that presented by the patient. Another brother has some type of mild "paralysis," which has been diagnosed as Chareot-Marie-Tooth type of paralysis. Another brother also has some type of undiagnosed paralysis. Their father had one foot amputated when he was still young, for some unknown cause.

The perforated lesion on the right sole is of four years' duration. It appeared first as a callus on the ball of the right foot, and it persisted for many years. About four years ago a tiny opening appeared, which refused to heal. Five months ago the lesion developed into the present ulceration. The patient says that the lesion is moderately painful at times. Previous treatment consisted of a sulfonamide gel preparation applied locally. Two radium treatments were given one year ago, which did not alter the appearance of the lesion.

On the ball of the right foot is a large callus. In the middle of this callus is a deep ulcer smaller than a dime in size, showing sluggish granulations and a slightly serous discharge. The callus and the ulcer are raised on a puffy, swollen base.

All deep tendon reflexes are normal. The roentgen ray examination of the foot showed old fractures of the third and fourth metatarsals with good osseous union.

The fourth metatarsal is somewhat shorter than normal. The great toe is angled outward, showing early formation of a bunion. There is no evidence of periostitis or of osteomyelitis. The Wassermann, Kline, Eagle and Hinton tests all elicited negative reactions. The blood sugar level was 86 mg per hundred cubic centimeters.

## DISCUSSION

DR NELSON PAUL ANDERSON. There is a definite indication of a familial tendency, and, while I do not believe that ordinary syringomyelia runs in families, there is a group of familial cases reported in the French literature. These cases occurred in a part of France, possibly Brittany, where a syringomyelia-like syndrome has been present in certain families for a hundred years. I believe that these presented cases belong in that category. They are examples of familial syringomyelia. The other member of the family who presents a Charcot-Marie-Tooth type of atrophy has a different clinical picture than that presented by the two women.

DR SAMUEL AYRES. These patients are interesting because they are sisters having similar lesions and they have brothers and a father who have paralysis and trophic disturbances of the lower extremities. In Wechsler's "Textbook on Clinical Neurology," fifth edition, the condition is described as a rather peculiar syndrome with a type of atrophy which is difficult to correlate with the underlying pathologic changes. Degeneration has been found in the posterior columns, in the anterior horns and roots and in the peripheral nerves. The disease is probably hereditary degenerative. It is commoner in men and may occur in several members of a family. Perforating ulcer of the foot is mentioned as one of the complications of the disease. The father of these patients at an early age had one foot amputated for some disorder, and the amputation wound remained chronic for many years. As far as diabetes is concerned, I think that it can be ruled out. The fasting blood sugar level was 86 mg per hundred cubic centimeters of blood. There is no obvious neurologic manifestation in either of the sisters presented.

## Book Reviews

**Human Torulosis** A Clinical, Pathological and Microbiological Study, with a Report of Thirteen Cases By Leonard B Cox, M D, and Jean C Tolhurst, M Sc Price, 25 shillings Pp 150, with 67 illustrations Melbourne Melbourne University Press, 1946

In this book the authors report 13 cases of torulosis of the central nervous system, in some of which the condition was associated with torulosis of the lungs and subcutaneous tissue, syphilis, Hodgkin's disease or pulmonary tuberculosis. The detailed study of their own material supplemented by a review of a large literature forms the basis for a discussion of torulosis of various organs, its signs, course, prognosis and differential diagnosis. This excellent study includes the central nervous system, the respiratory system, the lymphatic system, the skin and mucous membranes, the bones, the joints and other tissues. A special chapter is devoted to the microbiology of *Torula histolytica*, its structure in tissues and in cultures, its resistance to heat, its viability and its antigenic properties. Another chapter deals with experimental torulosis in animals—mice, rats, guinea pigs, rabbits, monkeys, cats and dogs. Pathologic changes of human and animal torulosis in various organs and tissues are described. The discussion of the laboratory diagnosis of the disease includes the technique of examination of cerebrospinal fluid, sputum, nasopharyngeal secretion, blood, urine and skin, the tests of the skin and the serologic reactions. In the last two chapters are the description of the sources and routes of infection and the treatment of the disease. Illustrations are excellent. There are numerous roentgenograms of the lungs and pictures of gross and microscopic specimens of various organs of human beings and animals with torulosis and of cultures of the fungus. This book contains a wealth of original observations and a systematic review of a large literature and is a most valuable contribution to the knowledge of this rare, grave and relatively little known disease.

## News and Comment

### GENERAL NEWS

A meeting of the Society for Investigative Dermatology will be held on June 10, 1947, at Atlantic City, N J.

### DEATHS

Dr Isaac R Pels died in Baltimore on Feb 4, 1947

Dr Ernest Dwight Chipman died on Dec 4, 1946

Dr Arthur Whitfield's death was announced in London, England, on Feb 4, 1947

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## LICHEN SCLEROSUS ET ATROPHICUS WITH BULLOUS LESIONS AND EXTENSIVE INVOLVEMENT

Report of a Case

HELEN RELLER GOITSCHALK, M D

AND

ZOLA K COOPER, Ph D

ST LOUIS

A CASE of lichen sclerosus et atrophicus is presented because of the extensive involvement of the skin and because of the numerous bullous lesions

The clinical and pathologic findings in lichen sclerosus et atrophicus were authoritatively presented by Montgomery and Hill<sup>1</sup> in 1940. They observed 46 patients with the disease and succeeded in distinguishing the clinical and histologic changes from those of morphea guttata and lichen planus atrophicus.

The characteristic clinical feature of lichen sclerosus et atrophicus is a white papule, which may be discrete or one of a group forming a plaque. On the surface of each papule is a dark plug, resembling a comedo, or a tiny depression which is the site of a former plug. Atrophy may occur in the later stages, with parchment-like wrinkling and greater prominence of the plugs.

According to Montgomery and Hill<sup>1</sup> the characteristic histologic features consist of relative and absolute hyperkeratosis, with keratotic plugging of the orifices of the hair follicles and dermal appendages; atrophy of the rest of the epidermis, with flattening and loss of the rete ridges, mild liquefaction degeneration of the basal layer, lymphedema in the upper portion of the cutis, with edematous changes in the connective tissue fibers beneath the epidermis, and a cellular infiltrate in the midcutis beneath the area of edema. There are no obliterative changes in the deeper blood vessels, such as occur in morphea guttata.

Myers<sup>2</sup> and Schubert<sup>3</sup> described patients with typical lichen sclerosus et atrophicus. Bullous formation was noted in their patients.

From the Dermatological Department and the Pathological Department of the Barnard Free Skin and Cancer Hospital and the Washington University School of Medicine.

1 Montgomery, H., and Hill, W. R. Lichen Sclerosus et Atrophicus, *Arch Dermat & Syph* **42** 755-779 (Nov.) 1940

2 Myers, W. K. Lichen Sclerosus Case Report, *Brit J Dermat* **48** 658-660 (Dec.) 1936

3 Schubert, M. Zur Kenntnis des Lichen sclerosus atrophicus, *Dermat Wchnschr* **103** 1653-1662 (Dec 19) 1936

Schubert stated that in his patient some of the patches were elevated above the surrounding skin and, after the insertion of a needle, a drop of clear yellow fluid was obtained. The histologic findings in both of these patients corresponded with those described by Montgomery and Hill,<sup>1</sup> who did not mention vesicle formation in any of their own cases.

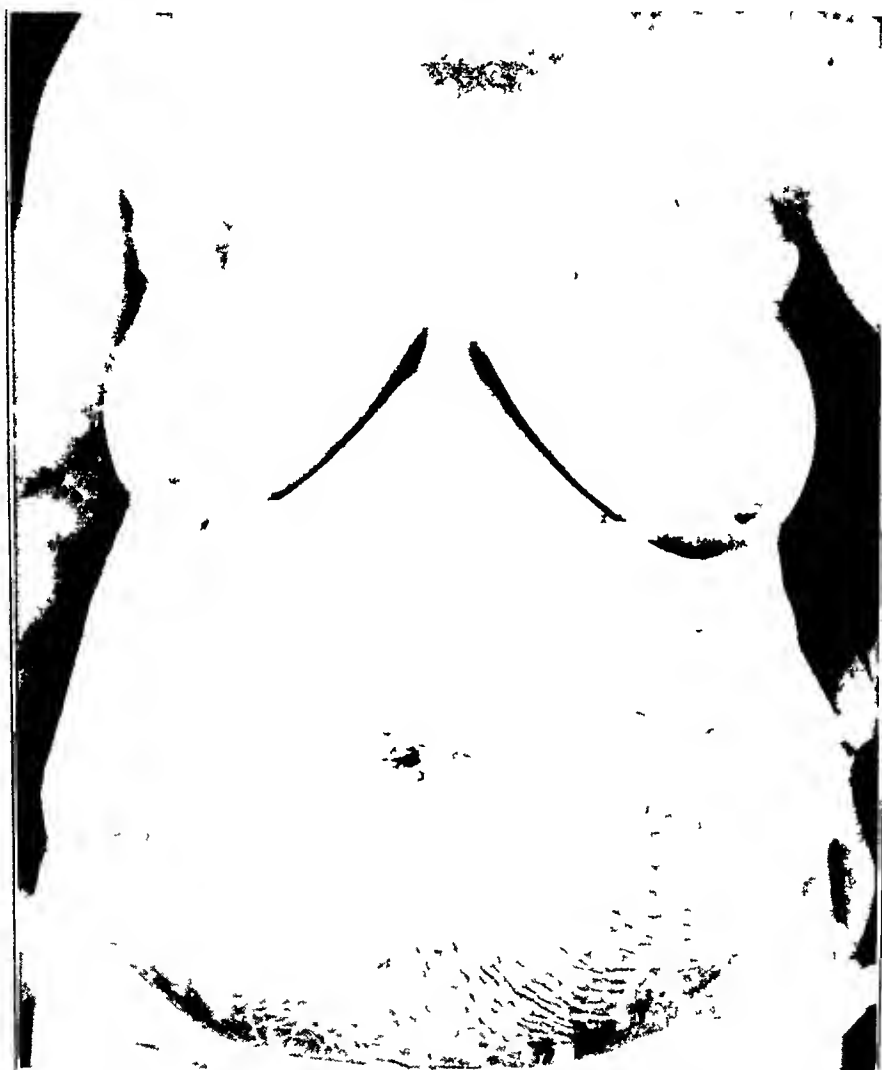


Fig 1—Pale, atrophic, ivory-colored skin over the lower part of the abdomen, studded with follicular plugs

but who stated that the edema in the upper cutis may be so great as to result in the formation of vesicles just beneath the epidermis. These vesicles may be apparent on clinical examination. Anderson<sup>4</sup> sum-

4 Anderson, G. R. Bullous Lichen Sclerosus et Atrophicus, *Arch Dermat & Syph* 49:423-426 (June) 1944

marized the reports of cases of lichen sclerosis et atrophicus with the formation of bullae and added 1 case. He thought that many of the conditions reported as localized scleroderma with bullous lesions were actually bullous lichen sclerosis et atrophicus.

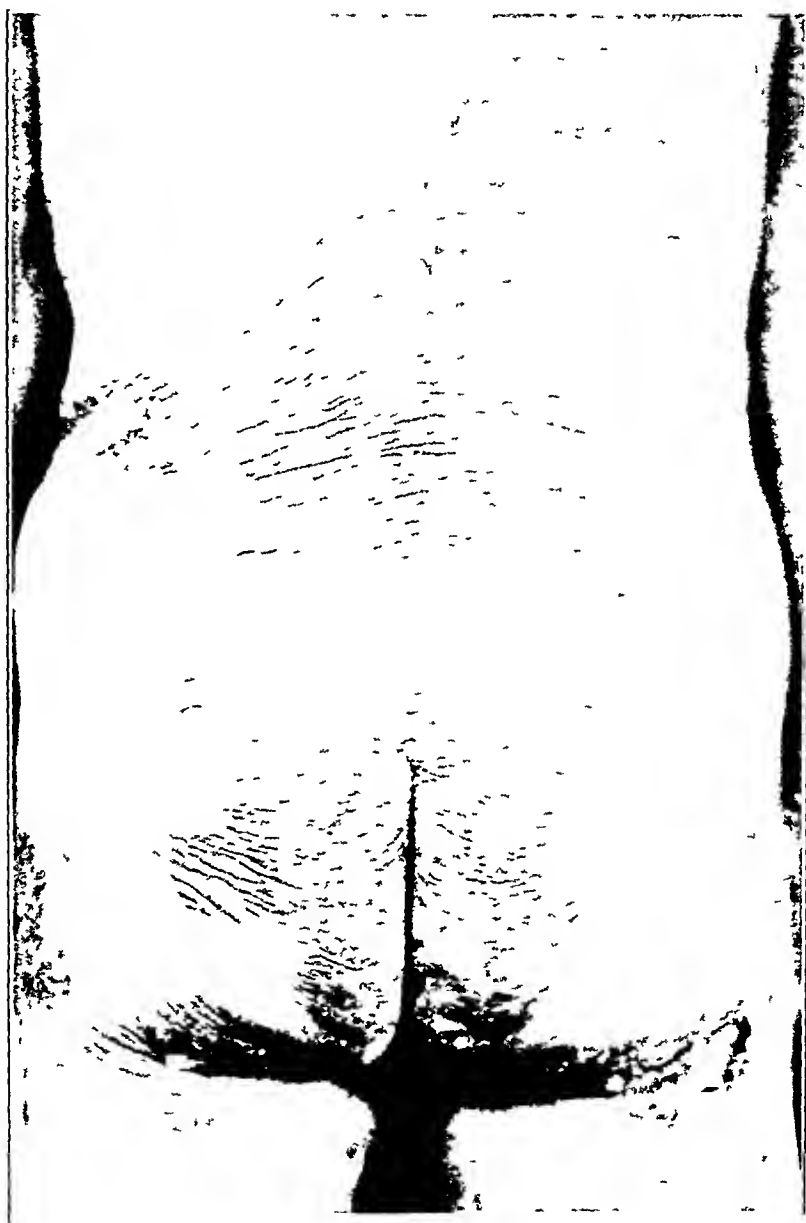


Fig 2—Atrophic skin and brownish pigmentation of the lower part of the back, with bullae in the folds below the buttocks and on the left flank

#### REPORT OF CASE

M. C., a 64 year old white woman, entered the clinic on Aug 14, 1944, complaining of "tightness" of the skin of the folds of the body of seven weeks' duration. The skin over the buttocks was so "tight" that she had not been able to sit for several weeks.

Examination revealed that the skin of the entire body except that of the face, hands and feet was dry and wrinkled. In the folds of the body, it was loose and moved easily over the deeper structures. The color was pale ivory under the breasts and over the abdomen (fig 1). About the spine and in a circular area



Fig 3—Lichen sclerosus et atrophicus. Section of a specimen from the abdomen, showing decided hyperkeratosis, atrophy of the rest of the epidermis, pronounced lymphedema at the junction of the dermis and epidermis, homogenization and edema of the connective tissue in the upper portion of the dermis and a cellular infiltrate in the midcutis. Hematoxylin and eosin  $\times 140$ .

about the anus, there was some brown pigmentation (fig 2). The color of the remainder of the skin appeared normal. Follicular plugs, resembling comedos and easily expressed, were especially noticeable on the ivory-colored skin of

the abdomen and chest. The folds of the labia minora were absent, and on the inner surfaces of the labia majora there were small patches of white, shiny skin. The distribution of hair was normal on the head, but there was no hair in the axillas and little on the labia majora. The nails were normal.

On August 28 a large raw area, 4 by 6 cm in diameter, was noted beneath the right breast. An antiseptic ointment was prescribed to be applied to this area twice daily. On September 4 large bullae were noted in the perianal region.



Fig 4—Lichen sclerosus et atrophicus. Section from the abdomen, showing preservation of the black-stained elastic tissue fibers and their separation from the epidermis by edema. Weigert stain.  $\times 175$ .

During the next week other bullae appeared on the abdomen, on the sides of the legs, in the fold below the buttocks and in the axillas (fig 2).

The patient was admitted to the hospital on September 21. Physical examination revealed a well developed, obese woman. The abnormal physical findings were limited to the changes in the skin except that one observer thought that he felt the tip of the spleen.

*Laboratory Data*—There were 3,890,000 red blood cells, 12.5 Gm of hemoglobin and 5,800 white blood cells, with 67 per cent polymorphonuclear leukocytes,

5 per cent stab forms, 2 per cent eosinophils, 22 per cent lymphocytes and 4 per cent monocytes. Sternal marrow puncture revealed that the bone marrow was hyperplastic with a slight increase in erythroid elements. The myeloid elements were normal. The eosinophils were increased, as were the plasma cells and clasmatocytes. The results of examination of the urine and stools were normal. The Kahn reaction was negative. The nonprotein nitrogen content was 16 mg per hundred cubic centimeters. The total protein content was 7.1 Gm per hundred cubic centimeters, with 4.2 Gm of albumin and 2.9 Gm of globulin. The cephalin-cholesterol flocculation test elicited a negative reaction. The blood cholesterol level was 208 mg per hundred cubic centimeters. The icterus index was 9. The blood sugar (fasting) content was 115 mg per hundred cubic centimeters. Gastric analysis showed 51 degrees of free acid. The basal metabolic rate was 0 and + 1 per cent. A series of roentgenograms of the gastrointestinal tract was reported as indeterminate. A roentgenogram of the chest showed aortic lengthening and peribronchial infiltration of indeterminate nature.

Biopsies were performed on specimens of the skin of the axilla and abdomen on September 28.

*Microscopic Description*—In the biopsy specimen from the axilla the epidermis showed pronounced hyperkeratosis, with plugging of the hair follicles and sweat gland ducts. The hyperkeratosis was so extensive that the keratin layer on the surface of the skin was more than twice as thick as the remaining layers of the epidermis below it. Except for this thickening of the stratum corneum the epidermis, as a whole, was so atrophic that it was composed of only two to three layers of cells. The rete pegs were completely obliterated. The granular layer, which was present throughout, consisted of only one row of extremely flattened cells. The cells of the squamous and basal layers were so compressed that they could scarcely be differentiated (fig. 3).

In the upper third of the dermis, there was so much edema that in places the epidermis was separated from the dermis by collections of fluid. The collagen fibers showed homogenization and edema. A Weigert stain revealed no destruction of the elastic tissue, but because of the edema the fibers were separated from the epidermis (fig. 4). In the center of the dermis there was an irregular band of cellular infiltrate, made up of lymphocytes together with a few plasma cells. This infiltrate was denser about hair follicles and blood vessels. The blood vessels of the dermis showed no obliterative changes. Hair follicles, sebaceous glands and sweat glands were still present. A biopsy specimen from the abdomen showed changes similar to those seen in the biopsy specimen from the axilla.

While visiting this clinic Dr. Hamilton Montgomery, of the Mayo Clinic, examined both the patient and the microscopic sections and agreed that this was a case of lichen sclerosus et atrophicus.

*Treatment*—While the patient was in the hospital, a soothing ointment (2 per cent ichthammol in 30 per cent paste of zinc oxide) was applied and infra-red irradiation was given to the ulcerated areas.

New bullae appeared on the inner sides of the legs and on the lower part of the back on November 20. Use of the ointment was discontinued, and 4 per cent bismuth tribromphenate in white petrolatum was applied. At weekly inter-

vals for four weeks the patient received roentgenologic treatments to the ulcerated areas beneath the breasts, in the axillas and on the legs and abdomen<sup>5</sup> The patient was discharged on December 19, with all the bullous lesions healed except those on the legs

She returned to the clinic at intervals of two weeks for further roentgenologic treatment to the lesions of the legs, which healed promptly after a total dose of 600 r had been given to them<sup>5</sup> On April 11, 1945 new bullae appeared in the right axilla and on the left knee, and on May 16, 1945 bullae appeared about the navel These areas healed promptly after roentgenologic treatment No new



Fig 5—Large area of superficial ulceration with bullae at the periphery over the left flank

bullae appeared until Sept 10, 1945 At that time a large area (10 by 12 cm) of superficial ulceration was noted over the left flank and side of the abdomen At the periphery of the lesion were many bullae (fig 5) This large area was almost completely healed on Oct 8, 1945, although only two roentgenologic treatments of 50 r each, two weeks apart, had been given

5 One hundred roentgen units each (85 kilovolts and 5 milliamperes through an 0.8 mm aluminum filter at a focal skin distance of 10 inches [25 cm]) was given

SUMMARY

A case of extensive, bullous lichen sclerosus et atrophicus is presented in which the clinical and histopathologic changes were identical with those previously described for this disease

The bullous lesions healed promptly after treatment with superficial roentgenologic therapy. There was a tendency for the bullous lesions to recur.

Washington and Theresa Avenues

## EXPERIENCES IN MILITARY DERMATOLOGY

Their Interpretation in Plans for Improved General Medical Care

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THE ARMED forces of the United States have completed one of the largest experiments in group medical practice that has ever been undertaken. Regardless of some errors which were made in scientific methods, in planning and in organization, it is believed that the history of the medical services will demonstrate conclusively that the individual soldier and sailor received medical and surgical care of a high standard. It is our purpose in this paper to assess, insofar as our individual experiences will allow, the successes and failures which dermatology, as one of the medical specialties, contributed to the over-all mission of prevention and cure of disease in the United States Army.

Official histories dealing with various aspects of the Medical Department of the Army will appear in due course. It is believed that these will be written objectively and honestly. They will furnish much information which should be of interest and value to students of military and civilian medical practice. In a short discussion written by two specialists in dermatology, it would be comforting, though dangerous and short-sighted, to be content merely with a listing of the accomplishments relating to dermatology during the war. However, we can state that during World War II, for the first time, dermatology was recognized as an important specialty in military medicine. Prior to mobilization of the Army, there was not a single qualified dermatologist in the Army Medical Corps, and Army hospitals did not include a department of dermatology. Throughout the war, it became increasingly apparent

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that cutaneous diseases constituted one of the major causes of disability and hospitalization and that specialized care of patients with these conditions resulted in a decrease of disability and hospitalization. Dermatology sections were, therefore, established in almost every hospital of more than eight hundred beds, and every effort was made to assign medical officers with special training in dermatology to these hospitals, insofar as such officers were available. Those who are responsible for the planning of graduate training of medical officers in the postwar medical corps are fully aware of the importance of diseases of the skin in military medicine, and plans have been formulated for graduate training of selected medical officers and utilization of civilian consultants to assist in this program.

While there is no intention to dwell on minor difficulties which were encountered, the clearcut demands of military medicine emphasized certain deficiencies in dermatologic knowledge and practice to a degree not always apparent in civilian life. Moreover, the place which dermatology occupies in medicine as a whole becomes more clearly evident in a large cooperative group effort than is the case in isolated private practice. There are serious gaps in the knowledge of diseases of the skin and, in our opinion, deficiencies of emphasis and effort in the investigation of problems related to disturbed states of the skin. They are our particular concern in this paper.

Many of the figures concerning the relative incidence of disease in various theaters of operation are not yet available. Nevertheless, certain statements concerning the chief problems in dermatology encountered in the Army may be made with accuracy. These will be considered under the following headings: (1) dermatologic disease as a source of disability in the Army, (2) planning and investigation to prevent and cure cutaneous diseases in the Army, (3) personnel (the utilization of medical officers with special training in diseases of the skin and the competence of general medical officers and of specialists in the management of dermatoses), (4) administrative problems in relation to dermatology, (5) the relation of dermatology to venereology, (6) cutaneous syndromes occurring with frequency in military practice (the chief advances in the prevention and cure of cutaneous diseases during the war years), and (7) the gaps in knowledge and errors in professional practice which led to increased dermatologic disability.

#### INCIDENCE OF DERMATOLOGIC DISEASE IN THE ARMY

Disability from diseases of the skin varies greatly in accordance with the climatic and hygienic conditions under which troops are living. The relative incidence in comparison with that of other medical diseases and of battle wounds also shows decided variation, largely dependent on the

prevalence of epidemic and endemic disease among the troops concerned and on whether or not they are engaged in active combat. In only one theater of operations, the European, did surgical admissions to hospitals exceed the medical admissions.

As stated previously, the admissions to the sick list for various types of disease and injury during the entire war have not yet been completely tabulated. However, data on the incidence of dermatologic disease in various large representative series are available. It should be kept in mind that all these figures apply to a group of young men, the diseases of women and of persons past the age of 50 are sparsely represented.

The admissions to Army hospitals primarily because of a cutaneous disease, in terms of dermatologic patients per hundred thousand troop strength per year in the Zone of the Interior and in various theaters of operation, are given in table 1.

TABLE 1—*Incidence of Cutaneous Disease in Various Theaters of War*

Place	Admission for a Cutaneous Disease per 100,000 Men in 1914
Zone of the Interior	5,551
North American Theater	3,731
Latin America	6,805
Mediterranean area	7,621
Middle East	10,399
Asiatic area	8,326
Pacific Ocean area	8,261
Southwest Pacific area	10,267

Admission rates for cutaneous diseases were approximately twice as great for troops overseas (80 patients admitted to the hospital per thousand men per year) as they were for troops in the United States (42 per thousand men per year). The duration of hospitalization of patients with diseases of the skin varied greatly but was often prolonged, as indicated by the fact that patients for whom transfer from an overseas station to the United States became necessary because of a cutaneous disease averaged a total stay in the hospital of five and a half months. In such patients, therefore, the period of hospitalization was of major order, of a duration which might be expected from a serious chronic medical disease or a severe injury incurred in battle.

Various other representative figures from hospitals in the European and Mediterranean theaters are available, as shown in table 2.

The incidence of cutaneous diseases in patients seeking treatment in an Army dispensary or outpatient department is difficult to determine accurately because it is frequently not feasible to preserve records on

these admissions. We have observed a large number of Army outpatient "clinics" of one type or another and have discussed the problem with numerous medical officers. It is estimated conservatively that between 15 and 25 per cent of all admissions to a dispensary or outpatient department in temperate climates are due to a disease of the skin. This percentage is increased by reason of overseas duty and a tropical climate and frequently reached 60 to 75 per cent of all patients seeking dispensary care.

The high incidence of cutaneous diseases in the Southwest Pacific area is well known. As representative of this, two examples of the disabling quality of such diseases may be cited. In an essential technical medical data report dated May 5, 1944, the following statement appeared:

TABLE 2—*Incidence of Cutaneous and Venereal Diseases in Different Areas*

Hospital	Total Admis- sions	Primary Diagnosis of Cutaneous Disease		Venereal Disease	
		No.	%	No.	%
Fifth General, North Ireland (1942)	7,040	468	6.6	395 (all types)	5.6
Tenth Station, North Ireland (1942)	2,000	101	10.0	131 (all types)	6.2
British Isles (Nov-Dec 1943)	14,408	1,015	7.2	422 (syphilis only)	2.9
Forty-Fifth General, Mediterranean (1944) (Manson, R. O., Kennedy, C. B., Buchanan, R. N., and Imhoff, R. F. Major Disease Problems in Natousa, report to the Surgeon General of the Army, 1944)	18,390	721	4.0		

"Diseases of the skin are an important factor in noneffective rates in the forward areas. Approximately 7 per cent of conditions in patients admitted to hospitals and about 4 per cent of conditions of patients evacuated to the United States are due to diseases of the skin. Many dispensaries show as high as 75 per cent of those reporting to sick call as suffering from disease of the skin." During the period Nov. 1, 1944 to Nov. 1, 1945, evacuation of approximately 14 to 16 per cent of all patients to the United States was due to diseases of the skin. Many were sent home because of a primary diagnosis of a cutaneous disease. In some months this was the most frequent cause of evacuation, with the exception of neuropsychiatric disorders, and in all months it was a more frequent cause of evacuation than battle casualties. In many general hospitals stationed in tropical overseas areas, the percentage of admissions to hospitals because of cutaneous disease increased to 15 to 20 per cent of the total during the latter part of 1944 and the first six months of 1945.

## INCIDENCE OF VARIOUS DISEASES OF THE SKIN

The types of cutaneous diseases seen varied considerably in different parts of the world, with the order of incidence varying in different areas and different military units

Overtreatment of inflammatory or parasitic diseases of the skin  
 Superficial pyogenic infections  
 Chronic eczematous eruptions of various types  
 Superficial fungous infections  
 Contact dermatitis from plants, uniforms, footgear and other material  
 Scabies  
 Insect bites  
 The quinaerine hydrochloride (atabrine) syndrome (chronic lichenoid and eczematoid dermatitis)  
 Diphtheria cutis  
 Seborrheic dermatitis  
 Warts, especially plantar  
 Extensive acne  
 Atopic dermatitis  
 Urticaria  
 Psoriasis

The entire group of "rare" dermatoses was of no significance in the total disability. It was a common complaint of dermatologists overseas that a major portion of the published dermatologic papers were of no practical value and little interest to them because the reports dealt at length with diseases which would be seen with great infrequency, even in a highly specialized dermatologic practice. It would seem that a disproportionate amount of time is spent in investigation of diseases which are responsible for an infinitesimal proportion of the total disability from dermatologic disease.

PLANNING AND INVESTIGATIONS TO PREVENT AND CURE  
 DISEASES OF THE SKIN IN THE ARMY

In any statement on prevention and cure in military dermatology during the recent war, it is difficult to comment constructively without being bluntly critical. The truth of the matter is that little attention was paid by the Army or its civilian advisory board, the National Research Council, to this problem until late in the war. The only exceptions were the projects of the Office of Scientific Research and Development on dermatophytosis, which were so ably conducted by Dr. J. Gardner Hopkins and his associates and Dr. Edmund Keeney and his group. The most significant contribution of organized civilian investigation in the prevention and treatment of cutaneous disease was that made by entomologists working under projects supported by grants recommended by the National Research Council. These investigators developed several compounds which were useful in the prevention of cutaneous disease caused by parasitic infestation and were chiefly responsible for the study and adoption of the Swiss compound DDT (4,4'-dichlorodiphenyltrichloroethane) for use by the armed forces.

In 1942, at the instigation of the Army and the Committee on Medicine of the National Research Council, the preparation of a simple manual

dealing with the diagnosis and treatment of cutaneous diseases commonly encountered in military medicine was undertaken. In view of the numerous excellent textbooks in dermatology, the need for such a manual might be questioned. However, it was apparent that many of the remedies recommended in textbooks were not available in the Army Supply Catalogue, nor was inclusion of most of them practically possible in view of the already enormous complexities of Army medical supply. Also—and this was a startling revelation to us—many physicians have had so little opportunity for dermatologic training in medical school and internship that they are unable to arrive at a diagnosis of even the simplest conditions of the skin. Working alone in isolated stations, they required help in arriving at a reasonable working diagnosis and proper simple treatment in any given case. With the cooperation of the Navy, such a manual was prepared and distributed widely throughout the armed forces.

In view of the large scale studies which were initiated on many special problems in other fields of medicine and surgery, it was a matter of some surprise to us that more studies were not undertaken in certain aspects of dermatology which had proved to be important sources of disability in other armies. These included particularly the prevention and cure of scabies, the general problems of drug sensitization, the prevention and cure of pyogenic infections, methods of protecting the skin against contact sensitization, the effects of a warm environment on the skin itself and the untoward effects of various drugs on the skin. As noted previously, late in the summer of 1942, fruitful studies on the prevention and treatment of fungous infections of the skin were initiated but there was no correlated study of superficial pyogenic infections until the summer of 1945. All these problems were, of course, under study in civilian institutions, but there was nothing even remotely comparable to the scope of official studies initiated on a wide variety of other diseases and hazards, many of which proved to be of far less significance as a source of disability than cutaneous diseases. This fact is not recorded in criticism, but rather to illustrate a curious scientific blind spot or indifference which many clinicians and scientists have toward experimental and clinical problems relating to the skin.

#### PERSONNEL

The utilization of specially qualified personnel in an army in the capacities for which they are best suited is a problem of great difficulty. Some of these difficulties are obvious, others do not become apparent until one has been charged with some responsibility for solving them. It seems obvious, on the basis of civilian experience, that any well trained specialist should be assigned where he can care for a considerable number of patients with diseases of which he has special knowledge. On the

other hand, the functions of many military hospitals changed rapidly at times and a general hospital with many patients presenting diseases of the skin might suddenly be designated as a special center for some type of surgical case and the dermatologic and other medical patients evacuated elsewhere. It was not easy to transfer the physician along with the patients, and indeed it was often unwise to do this as a temporary expedient.

Dermatologists, as medical officers in the broad sense, had certain nonmedical duties to perform as responsible persons in a military organization. Much criticism has been leveled against the necessity of too much of this, and some criticism was entirely justified. But one had only to see a few units composed primarily of medical specialists rather than of officers of the Army with special skills to realize the lack of organization, discipline and efficiency which could soon pervade such a unit with resultant poor care of patients. In addition, certain types of combat medical duty were so demanding physically as to make it essential that young medical officers, regardless of their special training, be assigned to such duty. Some dermatologists, because of opportunities for promotion or for special considerations, such as flight pay, elected to take assignments which involved purely administrative duties or that otherwise offered no opportunity for the practice of a specialty.

The peak number of medical officers in the Army was 48,319. Of this, there was a total of 137 officers in the Army with recognized competence in dermatology, i. e., an "A" or a "B" rating. Grade "A" and "B" dermatologists constituted the officers who had had recognized formal training in the specialty. Of this group of 137, 107 officers were possessors of certificates from the American Board of Dermatology and Syphilology, the remaining 30 had demonstrated such competence and had had sufficient formal training to justify a rating of "B". In addition, there was a group of 151 medical officers who had had a small amount of formal training in dermatology and who had demonstrated sufficient competence in the specialty to justify a rating of "C". These officers were ordinarily capable of being chief of a dermatologic service in a small hospital or one primarily concerned with the care of battle casualties. In addition, there was a considerable group of officers who had expressed an interest in dermatology but were generally without any training in the specialty except that which they had obtained in the Army. It is from this group that a considerable proportion of the veterans seeking graduate training in dermatology have been derived.

Of the group of 107 holders of certification in dermatology by the American Board of Dermatology and Syphilology, 102 were in posts offering an opportunity to do professional work in dermatology on V-E day. This favorable ratio was by no means representative of the

situation which prevailed in the early days of the war, it had been brought on by the increasing evidence throughout the war that dermatologic disease was responsible for much disability and by the efforts of persons in various headquarters<sup>1</sup> who were primarily interested in adequate professional service to patients

While there were many individual instances of officers with an interest in dermatology who had no opportunity to care for dermatologic patients, the situation of dermatologists was obviously far more favorable than that of gynecologists, obstetricians and pediatricians. War is no respecter of the lives or well-being of the persons engaged in it, and displacement of some specialists from their specialized professional pursuits is often unavoidable, though obviously wasteful and inefficient, as only war can be. Fortunately, with proper planning, such conditions can be avoided in times of peace.

Another striking feature of the management of cutaneous diseases in the Army was the incontrovertible fact that many students graduate from medical schools in the United States with only the haziest knowledge of dermatologic diagnosis and treatment. They have no real understanding of the ten or twelve groups of diseases of the skin which constitute over 95 per cent of the general practice of dermatology. In addition, they frequently have had no real opportunity to learn the indications and proper use of the few remedies which constitute the backbone of dermatologic therapy. It was a matter of considerable surprise to us that many highly trained and competent specialists in other fields particularly in internal medicine, had practically no knowledge and little interest in diseases of the skin. Some well trained internists have a good working knowledge of dermatology, but this was by no means the rule and constituted a striking deficiency of the training offered in some well known centers of internal medicine.

#### ADMINISTRATIVE PROBLEMS

It became increasingly evident throughout the war that one of the chief problems in furnishing good professional care was in bringing the patient and the physician best qualified to care for him together. The military ideal of a medical officer qualified to care for almost any-

1 In particular, our respective chiefs, Brigadier General Hugh J. Morgan, chief consultant in medicine to the Surgeon General, and Colonel William S. Middleton, chief consultant in medicine in the European Theater of Operation, did everything in their power to effect the best possible utilization of medical officers with recognized competence in dermatology and syphilology and to bring about a dermatologic consultant system in all major commands. It should be emphasized that this task was most difficult because tables of organization had not provided for such consultants.

thing from which a soldier might suffer was obviously a fanciful one, though stubbornly cherished by some administrators. While it was obvious that a soldier with a compound fracture of the femur would have to be removed as soon as feasible to a place where he could have expert care and rehabilitation, this was not so obvious in patients with chronic eczematous dermatitis or psoriasis. Because of the lack of appreciation by many administrators (particularly surgeons of armies in the field) and other physicians of the extreme importance of an accurate diagnosis and adequate early care of a patient with a disease of the skin, it was too often impossible to provide good treatment before the eruption had reached a phase which might require weeks or months of hospitalization before the soldier could be returned to duty. Obviously it was the function of commanding officers and medical administrators to keep as many men on duty as possible and to resist unwarranted removal of patients to hospitals farther back in the lines of communication, and a delicate balance had to be struck between medical and military demands.

The decisions as to whether or not a soldier with a cutaneous disease should be evacuated to a hospital in the rear or in another case whether he should be allowed to go overseas or whether he should be placed on limited duty were often difficult to make. It was in this phase of medical military administration that well qualified dermatologists were of the greatest value. Accurate diagnosis and a "sense" as to the prognosis in the individual case were essential. The value of adequate modern long term graduate training in the development of persons capable of making such decisions was repeatedly apparent in the Army.

Another phase of military dermatology which developed gradually during the war and in which the policy in various service commands, theaters of operation and armies varied greatly was in the facilities for consultation and special treatment which were made available. This depended to a great extent on the recognition by the responsible commanding officer that dermatologic disease was capable of causing considerable disability and on the advice of his medical consultant that something could be done about its prevention and cure, chiefly by way of furnishing adequate consultative and special treatment facilities. In the European Theater of Operations a Division of the Chief Surgeon was established in 1942, in which various branches of medicine and surgery, including dermatology, were represented by full time consultants. In the Office of the Surgeon General, on the other hand, dermatology was not represented in the Medical Consultants Division until March 1945, an almost unbelievable circumstance in view of the crisis in dermatologic disability which had gradually been gathering force in the various Pacific theaters for some time during the previous three years. A full time adviser or consultant in dermatology was available in one of the Pacific theaters, but not until 1943 (Dr John V Ambler). The need

A factor of great importance in dermatology as well as in other branches of medicine during the war was the facility with which information on technical matters was transmitted. It would seem a simple procedure to classify such material properly as to its confidential nature and send it through proper channels for the information of the authority concerned. It was nothing of the sort. Commanding generals of theaters of operation may dispatch or withhold information as they please within certain limits, and they or their deputies were often pre-emptory and unreasonable in their rulings on the transmissibility of certain technical information. In part, at least, physicians were responsible for this attitude, because of their inclusion in technical data of material which was primarily a function of command. Eventually the situation became clarified, and it was possible to transmit information on new diseases and their methods of treatment easily through technical medical data reports and direct technical channels. Before this was accomplished, however, the enormous value of prompt dissemination of information was realized more keenly than ever by medical officers overseas. In connection with this matter, it may be pointed out that delays in dissemination of information for the better care of patients are not peculiar to military organizations, civilian medical journals are often far from satisfactory in this regard.

#### RELATION OF DERMATOLOGY AND VENEREOLOGY

The prevention and treatment of venereal diseases in the Army were under the direction of the Division of Preventive Medicine and the Medical Consultants Division. It was well done, the advice of the National Research Council in the improvement of methods of treatment of gonorrhea, syphilis and other venereal diseases was adopted, and improvements in treatment were rapidly incorporated into Army practice. The introduction of penicillin therapy resulted in a phenomenal decrease in man-days lost by reason of venereal disease.

Since dermatologists have ordinarily had more experience in the early diagnosis of syphilis and of ulcerative lesions of the genitalia than any other single group in medicine, it was inevitable that many large venereal disease services were placed in charge of dermatologists. The chief of the Venereal Disease Section of the Division of Preventive Medicine of the Office of the Surgeon General during the last two years of the war was a dermatologist (Dr. Thomas H. Sternberg). The consultant in dermatology in the European Theater was responsible for the policies of treatment of all venereal disease, including gonorrhea. Many physicians without previous experience became relatively proficient in the diagnosis of venereal disease. It is our opinion, however, that proficiency in the diagnosis of ulcerative lesions of the anogenital region is not something which can be acquired by a short course of training. Accuracy in diagnosis is acquired only by prolonged experience under

close supervision, and dermatologists trained in some graduate centers though not all, were ordinarily efficient in the management of large numbers of patients with early venereal disease

The widespread employment of dermatologists in venereal disease clinics was worth while from the military standpoint, but we are not convinced that it is advantageous in civilian life. Certainly it was often a waste of medical talent to place highly qualified specialists in positions in which they were called on to do a large amount of work on the prevention of venereal disease. Many of the methods of prevention of venereal disease are, in our opinion, of doubtful, or at least not demonstrable, value and require little technical knowledge for their prosecution. The basic problem of control of venereal disease is dependent on factors far beyond the scope of condoms, V packets, suppression of or cooperation with houses of prostitution, management of prophylactic stations and lectures on sex.

The field of syphilis is one which inevitably enlists the interest of specialists of many different types. A knowledge of dermatology must include a thorough knowledge and proficiency in the methods of diagnosis of the ulcerative and cutaneous lesions of syphilis, and many dermatologists will retain an interest in all phases of syphilis. Nevertheless the management of large clinics for treatment of syphilis involves a great expenditure of time and effort, and it is our belief that this frequently results in too little effort in the study of difficult clinical and investigative problems of the skin. The study of methods of treatment of syphilis is now being prosecuted on a long term national scale, with adequate funds. It is certain that nothing resembling this in terms of organization and effort is being devoted to dermatology, and it is our opinion that this inequality will be made up only by the efforts of physicians interested in dermatology in presenting the problems clearly, in obtaining support for their solution and in prosecuting investigative work which will earn the respect of medicine as a whole.

In the British army, dermatology and venereology have been entirely dissociated. With proper centralization of patients, this results in no increase in the physicians necessary. One of us had an opportunity to observe this system in detail and came to the conclusion that there is much to recommend it. As they have in the past, some dermatologists will continue to contribute brilliantly to the field of syphilology, but we are by no means convinced that continuance of a primary interest in syphilis for all dermatologists is advantageous for progress in the better understanding of diseases of the skin.

#### CHIEF ADVANCES IN DERMATOLOGIC DIAGNOSIS AND TREATMENT OCCURRING DURING THE WAR

Unusual syndromes which occurred with considerable frequency included the following conditions. 1 Drug eruption due to quinacrine

hydrochloride occurred frequently, the cutaneous lesions of which were lichenoid and eczematoid patches of characteristic type, with exacerbations of generalized exfoliative dermatitis in some patients and, rarely, aplastic anemia and hepatitis. Reports describing this disease and its probable causation were first submitted to the Surgeon General from the Southwest Pacific Theater by Schmitt<sup>2</sup> and Nisbet<sup>3</sup>. Later, world-wide Army experience made it evident that this disease occurred only in overseas areas where quinacrine hydrochloride was used for the suppressive treatment of malaria, and it was established by many observers that essentially it is a drug eruption caused by quinacrine hydrochloride, although it is probable that climatic and geographic factors are contributing factors, because the incidence was much greater in New Guinea and adjacent islands and in Assam. It has been referred to as atypical lichen planus, lichenoid and eczematoid dermatitis syndrome and quinacrine hydrochloride dermatitis complex. Some observers have not included in the syndrome the eczematoid lesions not accompanied with lichenoid lesions. It is our opinion that this syndrome is a characteristic drug eruption essentially due to quinacrine hydrochloride and manifested by (1) a combination of lichenoid and eczematoid lesions, (2) lesions not accompanied with eczematoid lesions and (3) a particular type of eczematoid dermatitis which is symmetric and with a predilection for the hands and feet which can be usually distinguished from other types of eczematous eruptions by experienced observers. It seems preferable to include all these manifestations in one group and refer to it as quinacrine hydrochloride dermatitis. Accurate figures on incidence are not available. It is probable that at least 1 per cent of all persons in hot, humid, tropical overseas areas who took quinacrine hydrochloride in suppressive dosage over a period of at least six months acquired some type of cutaneous reaction. A small number of these patients have permanent hypersensitization and/or atrophy, and in some instances the eczematoid lesions persist or recur for long periods.

2 Diphtheria of the skin occurred particularly in the Pacific and China-Burma theaters and was responsible for much disability and some deaths. Essentially, cutaneous diphtheria is a tropical disease and one that occurred in epidemic form only in persons who were under combat conditions, with all that this implies in regard to poor personal hygiene, cutaneous injury and close personal contact. For the most part, it is an ulcerative process on the skin, characterized by

2 Schmitt, C. L., Alpins, O., and Chambers, G. Clinical Investigation of a New Cutaneous Entity, *Arch Dermat & Syph* 52 226-238 (Oct) 1945

3 Nisbet, T. W. A New Cutaneous Syndrome Occurring in New Guinea and Adjacent Islands. Preliminary Report, *Arch Dermat & Syph* 52 221-225 (Oct) 1945

ulcerative lesions covered either with a grayish, yellowish or brownish gray membrane or with a black or brownish adherent leathery slough, which separates after variable periods, resulting in sharply punched-out indolent ulcers which heal slowly, leaving thin atrophic scars, which frequently break down spontaneously or on slight trauma. In a few cases the disease occurred on an indolent eczematous plaque which was difficult to distinguish from other eczematous lesions. The management of cutaneous diphtheria is in every respect similar to that of faucial diphtheria, namely, early diagnosis, isolation, early administration of diphtheria antitoxin and observation for cardiac and neuritic complications. The predilection of *Corynebacterium diphtheriae* for the skin under hot, humid, tropical climatic conditions is most interesting, and an adequate explanation for this curious phenomenon might shed light on the occurrence and course of other bacterial infections of the skin under different climatic conditions.

3 Scabies and its sequelae were frequently seen. Medical officers in the European Theater cared for large numbers of patients with scabies, a disease which was endemic in the British Isles and in France during the war. In connection with this disease, the deficiencies of the American medical educational situation in respect to dermatology were strikingly apparent, most medical officers had no concept whatever of the chief diagnostic features of scabies, and little knowledge of its treatment. The disease was under intensive study in the United Kingdom during the war, and the results of these studies, particularly that by Mellanby,<sup>4</sup> were of great value in meeting the situation.

4 Better understanding was gained of the variety of effects which a warm climate and excessive sweating may have on the human skin.

5 There were many additions to the wide variety of substances capable of producing contact dermatitis.

Among the most valuable advances in prevention and treatment may be listed the following ones:

1 DDT was introduced, by means of which pediculosis corporis became almost nonexistent in soldiers. This compound was also of great value in the treatment of pediculosis pubis, which had previously been responsible for a considerable amount of disability because of improper, irritating methods of treatment. The effect of DDT on fleas and some other parasites was only moderately satisfactory.

2 Penicillin was introduced in the treatment of pyogenic dermatoses. In the Army, as elsewhere, this produced extremely rapid cures of many pyogenic infections which had resisted other methods of treatment. It soon became evident, however, that this method of

<sup>4</sup> Mellanby, K. Transmission of Scabies, *Brit. M. J.* 2 405-406 (Sept. 20) 1941. Scabies, New York, Oxford University Press, 1942.

treatment had shortcomings and that its local use was accompanied with a considerable incidence of contact sensitivity reactions

3 Use of nonirritating higher fatty acids was more widespread in the prevention and treatment of superficial fungous infections. The limitations of such compounds have not yet been entirely established. However, they undoubtedly constitute a significant advance in that they afford a reasonably effective, nonirritating method of treatment. The importance of individual hygiene of the feet and the inefficiency of prophylactic baths of the feet in the prevention of fungous infections of the feet became evident. The use of prophylactic baths of the feet has been discontinued in the Army. In particular, the work of Dr J. Gardner Hopkins and his associates established certain facts in regard to the incidence, prevention and treatment of superficial fungous infections which made it possible for the Medical Department to adopt a more rational approach to the control of this group of diseases.

4 Resin of podophyllum was introduced in the treatment of venereal warts. This is superior to any other method, in our experience.

5 In syphilology, the introduction of penicillin therapy into Army practice was important. This was first used on a large scale in the European Theater, starting June 26, 1944. It is doubtful that the demands of war in combat areas would have permitted anything approaching adequate treatment of syphilis by any other method.

6 Benzyl benzoate therapy for scabies was introduced. This method of treatment, though not without certain shortcomings, was superior to sulfur therapy for outpatient treatment.

#### GAPS IN KNOWLEDGE WHICH LED TO INCREASED DERMATOLOGIC DISABILITY

The urgent demands of conditions obtaining in combat zones sharply emphasized certain deficiencies in the available methods of dermatologic therapy. At times, the shortage of hospital beds became acute. Also, the allowable period for treatment of patients in the combat area was brief at times, and this often brought the inefficiency of treatments for some cutaneous disease to administrative attention.

The unsolved problems in dermatologic therapy which were most obvious were as follows:

1 Means of controlling chronic pyogenic or fungous infections and of reducing a patient's sensitivity to the bacteria and fungi which become an almost irremovable part of his skin flora were inadequate. We believe that cutaneous pyogenic infections are far more important causes of chronic disabling diseases of the skin than are superficial fungous infections.

2 Methods of controlling itching were inadequate Why should there not be an antipruritic agent as satisfactory, for instance, as hypnotic agents for the control of insomnia?

3 There was a lack of knowledge concerning chronic eczematous eruptions of the hands and feet, and the relative slowness and inefficiency of methods of dealing with them presented problems

4 Physicians lacked means of controlling excessive perspiration and methods of protecting the skin from its deleterious effects

5 Methods of preventing the harmful effects of prolonged residence in tropical climates on the skin were inadequate

6 There was a lack of any simple certain method of protecting the skin against contact dermatitis from plants and other contactants

7 There was a relative lack of satisfactory methods of controlling acute noninfectious inflammatory reactions of the skin rapidly and safely

8 Methods of treating warts, especially plantar warts, were cumbersome and unsatisfactory

9 Methods of dealing with chronic allergic states involving the skin, especially in persons whose environment and diet could not be adjusted to their particular sensitivities, were slow and unsatisfactory

10 There was a relative lack of scientific approaches to the study and management of psychosomatic states in chronic dermatoses

11 Methods of treatment of severe acne were slow and tedious

12 The intractibility of psoriasis, which almost always became worse in an overseas environment, presented a problem

13 There was a relative lack of knowledge of the basic factors in seborrheic dermatitis, which also frequently became severe in men overseas

#### CONCLUSION

It is believed that the experiences of the war emphasized to many physicians that dermatoses are an important source of disability and that their knowledge of dermatology was often inadequate It is believed, also, that a considerable number of physicians were impressed by the efficiency of certain specialized methods of treatment, especially when based on sound scientific grounds Also dermatologists with an adequate knowledge of internal medicine were more successful in treatment than those with a purely "externist" approach With these considerations in mind, it is our opinion that the following approaches to better care of the dermatologic patient are of great importance

1 More adequate time must be devoted to the teaching of dermatology in medical schools Better pedagogic methods must be employed with greater emphasis on the recognition and management

of the common dermatoses and of the dermatoses of general medical significance

2 It is believed that the advisability of complete separation of dermatology and syphilology in larger medical centers should be considered

3 Graduate students should be encouraged along lines of basic laboratory studies in the physiology of the skin and of the relation of disturbances of general body metabolism to changes in the skin

4 The interest of investigators in the basic sciences in the problems of clinical dermatology must be stimulated and active cooperation given to them by clinicians

5 More private and state funds must be enlisted in the adequate support of numerous problems in dermatology which are of great importance in the efficiency and well-being of a considerable segment of the population

6 It is felt that the externist approach in dermatology is dangerous and inefficient and that graduate training in dermatology should include adequate experience in internal medicine, with close cooperation between departments of internal medicine and of dermatology. The knowledge of many well trained internists is often strikingly deficient in regard to diseases of the skin, and the specialty training of internists would be improved by instruction in the rudiments of dermatology

#### DISCUSSION

DR MARION B. SULZBERGER, New York. I am not the only member of the Navy Medical Corps who is here, nor am I the official spokesman for the Navy Medical Corps, but I should like to say one word in emphatic endorsement of every comma and every inflection of what Dr Pillsbury and Dr Livingood have just presented. I do not know a single important point at which the naval experience differs from theirs. Certainly my personal observations do not differ from theirs, nor would my conclusions differ from those they have drawn. The figures given for the Army coincide almost to the third decimal place with those which the Navy compiled regarding the incidence of cutaneous diseases in various theaters and which have been repeatedly published and emphasized, and the reaction of the average nondermatologic naval medical officer to the tremendous problems of the recognition and management of cutaneous disease was identical with the reaction which is here described on the part of the Army medical officers.

The one fact which I would like to express most strongly is that the authentic and lively interest which has been aroused by this high incidence of cutaneous diseases and by the recognition of their ignorance on the part of the medical officers who were for the first time brought face to face with these cutaneous diseases really affords a golden opportunity for development of dermatology. If facilities for teaching can be expanded both in undergraduate and in postgraduate medical schools and if the situation can be brought to its deserved public attention, so that the general medical and public interest will keep pace and reach the same level as it has attained in these young medical officers, there are both the chance and the obligation to train more and better men in this specialty than was ever possible before.

I should like to say a word with regard to the plans of Admiral McIntire, Admiral Harper and Captain Newhouser for the Navy's postgraduate education in dermatology. The plan is now pretty well ripe, and at this point it may be described as follows. Outstanding reserve officers of the Navy are serving on a consultants board, one representative of each major specialty, and on this board dermatology is included. This board has the task of organizing, directing and being a recommending body to the Surgeon General regarding postgraduate medical education for medical officers of the regular Navy. The plan for dermatology is to have a certain number of medical officers of the regular Navy assigned each year to civilian institutions recognized by the American board for training—full time training—in dermatology and syphilology. That training will be supplemented by residency type training in fully equipped and staffed dermatologic centers which are being established at present at Naval hospitals and which we hope will meet the requirements of the board of certification.

One such center has been tentatively approved at Philadelphia, as Dr Lewis and Dr Gilman and others here know. A second one now is being organized and will apply for approval at St Albans, N Y. It is contemplated that more dermatologic centers will be established, particularly on the west coast, as time goes on. The present plan is, therefore, to give regular Naval medical officers the best available training both outside and inside the Naval hospitals and thus try to develop them into teachers, so that the deficit which the Navy now feels in its lack of medical officers certified in dermatology will be filled as expeditiously, adequately and uninterruptedly as possible.

DR HAROLD N COLE, Cleveland. I recently received a copy of the Rockefeller Foundation report, I read it over with a great deal of interest and immediately sat down and wrote Allen Gregg and told him that I noted appropriations for this and appropriations for that and that, as usual, there was nothing done for dermatology in this country. Then I mentioned the experience of my own hospital unit, University Hospital Unit 4, which was the first one out of the country and which was sent down to Australia.

Fortunately, my colleagues and I had gotten in a provision in this unit that one of our men was in the unit as a dermatologist, and Dr Frank McDonald has told me his experiences. He went down to Australia. They had anywhere from 10 to 20 per cent of the complete bed capacity devoted to dermatology. After they had been down there a while, a unit from another large university—a celebrated university in this country—was sent down to that same island. It did not have a dermatologist, and after it had been there a while some of the men came over to University Hospital Unit 4 and asked whether it would not be possible for one of them to come over there two or three times a week and make the rounds because they were getting nowhere in the care of their patients and it did not look as if they would be able to get a man down there to take care of this material.

Then the hospital unit was sent up to New Guinea. A large part of this hospital was supposed to be devoted to surgery. Most of the time that this unit was in New Guinea, 20 to 40 per cent of the one thousand beds were devoted to patients with dermatologic disease. That indicates exactly what Dr Pillsbury has brought out.

It is unfortunate that more prominence is not given to dermatology in medical schools. It takes a great war to bring out its importance. It was true in World War I, and particularly so in the war just finished.

I think that dermatologists owe a great deal to Dr Sulzberger for the way the Navy handled the problem. He was able to get in early and establish a correct

recognition of the specialty's importance. Moreover, I hate to think what would have happened in the Army medical service in the European Theater so far as dermatology is concerned if it had not been for Donald Pillsbury.

DR C GUY LANE, Boston. I have naturally been much interested in this paper, and, as a representative of World War I, I am willing to confirm all that Dr Pillsbury has said about this war, especially that dermatology is of significance because of the disability caused by dermatologic disturbances. To prove that to some of the medical officers who were assigned to Massachusetts General Hospital in the early part of the war, I drew up two tables. One of them shows the number of cases of cutaneous disease in the last war, as obtained from the statistics of the Surgeon General's Office. It is hard to believe that these figures show all the cases. It would seem that there were more than 126,000 cases of cutaneous disease. If one looks at the number of patients with dermatitis on the chart, one sees only 5,000 patients hospitalized, there must have been more than that. Take the cases of fungous infections, there must have been more than are itemized here. The other slide shows the number of days' disability, and these are simply those concerned with patients admitted to hospitals. Of course, scabies and cutaneous infections present the larger figures, as they do today. These figures, together with the figures from this war, are a forceful argument for better training in this field of medicine.

Secondly, he called attention to the mismanagement of ailments of the skin as a factor in the cause of disability in the Army. Dermatologists are all seeing that in clinics and in practice every single day.

He also called attention to the lack of knowledge, or perhaps it is a failure to use the knowledge which they have. I think that all the dermatologists who are conducting examinations for the American Board of Dermatology and Syphilology will bear that out. It has certainly been discouraging to me at times in quizzing students with regard to the fifteen or twenty common diseases, to find their extreme lack of knowledge with regard to characteristics, differential diagnosis and therapy.

He spoke of the lack of even minimal training in dermatology among medical officers. This has been of considerable concern to me personally, because Harvard Medical School allows me only five lectures a year to cover the whole field of cutaneous disease and allows ten or eleven two hour periods in the clinic for small sections.

Then he spoke about the matter of specialists in other fields not having instruction in dermatology. That is true. There is too little contact in general with other fields, especially internal medicine.

These five items, it seems to me, represent five indictments of dermatology in general, and something ought to be done about it. I suggest that a survey be made by a committee on education, to be appointed by the American Dermatological Association, or perhaps by a joint committee of the American Dermatological Association and the American Academy of Dermatology and Syphilology. Such a committee should survey dermatologic teaching throughout the country and review methods of teaching. Perhaps it can develop some standards of adequate graduate instruction and provide the various chiefs of dermatologic departments with material for use as arguments to procure more adequate teaching in this specialty. Such a committee would have an even larger field in the consideration of graduate courses in dermatology for general physicians and perhaps even the matter of education of the laity in dermatologic matters. We are all so much interested in the scientific aspects of clinical and laboratory dermatology that we are apt to pay little attention to these relationships, but in

this period of change it is time to give some thought to our public relations with medical schools, with physicians in other fields and perhaps even with nonmedical persons

DR C F LEHMANN, San Antonio, Texas It is certainly an appropriate time to bring this subject up I know of the many difficulties that Dr Pillsbury has had, and I am surprised that he can stand here with the composure that he manifested and give us such an unbiased, unexcitable sort of discussion of the problems that he encountered

I certainly endorse everything he said about training and giving more attention to dermatology in our medical schools I think, however, that a great deal of blame should be put on the Army for not recognizing the importance of this The lessons were learned in the other war I am one of those who at the outset of this war volunteered early and went in a general hospital—one of the largest—in which dermatology was a part of urology This sorry state of affairs was corrected as quickly as possible, and the Army had some excellent men in it who saw the need, however, owing to the huge task of building up far greater problems in dermatology and the cumbersome methods that were used, the evils were not corrected, but now is the time to correct those evils for the next war

I think that the solving of these problems that have been brought out will depend more on the establishment by the Army of dermatologic centers and training centers for the Army in which not only dermatologists but technicians, nursing force and other specialists are trained Dr Pillsbury did not tell you of the difficulties that I am sure he has had (because I have seen it) with the rapid shifting of personnel—trained personnel, trained to carry out a specific task and for some reason or other transferred rapidly Any one who has had any Army experience knows how that disintegrates a well established force, and in medicine it cannot be mechanized as it can in the artillery or the infantry

Another evil that will be seen—a costly evil—from this sore lack of the proper culling, the proper handling of dermatologic cases, is the tremendous amount of claims in the Veterans Bureau, claims of aggravation while in service of diseases that existed prior to service I am sure that all of the members are going to have to assume some responsibility as being watchdogs for the Treasury

DR GEORGE M LEWIS, New York I should like to ask Dr Pillsbury if in closing, he would develop the thesis that he mentioned in regard to separation of syphilis from dermatology This is a question that is being considered in certain quarters, and I think that at this time we should be interested to have him elaborate just a little on his recommendation

DR DONALD M PILLSBURY, Philadelphia There is a disposition on the part of the Army, Navy and the Public Health Service to train some of their career medical officers in the specialties I should like to speak for the cooperation of all training centers of dermatology in aiding such a program

In regard to the remarks of Dr Cole and Dr Lane about general hospitals going overseas without any attempt to include a person trained in dermatology among their personnel, I am certain that all such hospitals now recognize that this was a mistake I have discussed this with a number of medical chiefs of such hospitals, and they stated frankly that they had never realized the amount of hospitalization which could result from some of the simple dermatologic diseases Such hospitals, however, often furnished an enjoyable day for a visiting consultant I recall one unit, an excellent one from a well known medical center, which had no one in it with any real experience in dermatology Patients with various cutaneous diseases were scattered throughout many wards, and the standard

of dermatologic misdiagnosis was remarkable to behold. Among the group of extremely keen medical officers attached to this unit, I dare say that there was hardly one who could pass the examination in dermatology given to junior students. In the medical school which they had attended, dermatology had been deemphasized almost to the point of extinction.

Dr Lehmann mentioned a problem which will arise in connection with the care of veterans. Like many other returned medical officers, I am much interested in this and am sure of the desire of every one concerned to help in whatever way possible. The reorganization of the Medical Department of the Veterans Administration now in progress gives hope of an eventual high standard of professional care to veterans. Dermatology and syphilology is represented by a consultant in each of the thirteen branch sections, and it is hoped that an adequate service in this specialty will be available in all the general hospitals. There is great need, from the standpoint of better professional care to the veteran for the establishment of approved residencies in dermatology in some of the larger Veterans Administration hospitals. In the hospitals being staffed under the direction of the various dean's committees, there is no reason why this should not be accomplished in many places in the near future. Adequate liaison with the various specialty boards is being established and it is hoped that certification or training centers which deserve approval will be rapidly accomplished.

Dr Lewis has requested that I develop the thesis of the advisability of separating dermatology and syphilology a little further. In mentioning it before this group, I feel somewhat like a prodigal son who has come home and suggested that a part of the family plantation be sold. I have no doubt that many dermatologists will, as they have in the past, continue to be interested in all phases of syphilis and to participate effectively in the evaluation of the best methods of treatment of the disease. It is perfectly obvious that any competent dermatologist must be entirely familiar with the mucocutaneous lesions of early and late syphilis and with all the methods of diagnosis of the disease, both laboratory and clinical. However, I believe that in many departments of dermatology and syphilology, particularly those operating with limited personnel a disproportionate amount of time and energy is spent on the running of routine clinics for syphilis, to the detriment of adequate study of patients with dermatologic problems. It is my own feeling that the problems relating to disturbance of the skin are so common and so varied as to demand much more attention than they have hitherto received in this country. The long term studies designed to determine the best method of treating syphilis, being carried out under the auspices of the National Institute of Health are splendidly organized and are well supported financially. Compared with this study and the study of diseases such as tuberculosis and infantile paralysis, the support available for studies designed to reduce disability in the population resulting from cutaneous diseases is pitifully inadequate.

## MOELLER'S GLOSSITIS

A Case with Remission During Pregnancy

HERBERT RAINER, M D  
CHICAGO

**D**URING the meeting of the American Dermatological Association in Chicago in 1944, I presented at the clinical session a patient of mine with lesions on the tongue which were so unusual in character that a precise classification could not be made. The clinical picture suggested several diagnoses—aphthous stomatitis, drug sensitization, facitious glossitis and Moeller's glossitis.

### REPORT OF A CASE

The patient, a young married woman aged 23 years, complained of burning, painful areas on her tongue. These lesions were first noticed five years previously, and they had been present continuously since then except during the period when she was pregnant in 1941. Her tongue was free of symptoms for the entire nine months' course of her pregnancy. Aside from this remission the symptoms were present constantly, but the intensity of the pain and burning sensations would vary in degree from time to time. The acute phases seemed to occur in cycles of approximately three weeks, beginning about one week prior to the onset of a menstrual period, increasing in severity for some ten days and then subsiding somewhat one week after the menses. Throughout the acute stages her tongue would become so sensitive that the process of eating was a chore. Hot and spicy foods were especially aggravating, and even bland foods caused some distress. The mere act of talking was so painful that a naturally agile tongue was slowed down considerably. The patient noticed no unusual change in her weight, and there were no other evidences of harmful effects on her general health. There was no interference with sleep, and, surprisingly enough, in view of the constant discomfort in her tongue, there was no adverse effect on her disposition. The patient was a rather pleasant, placid person, who understood and cooperated intelligently with all efforts to solve her problem, and there was nothing in her manner or reactions that suggested that she was neurotic.

An examination of the tongue revealed that there were several sharply defined areas on the dorsum and sides that were exceedingly tender. Some of the lesions were paler than normal tissue, others were beefy red. They were all eroded, with shiny glazed surfaces that appeared to be swollen. The lesions were small (dime sized) and for the most part regular in shape, either rounded or oval. A few, however, had irregular shapes, with a tendency toward the bizarre, i. e., with sharply pointed angular borders or with stripes. The color of the lesions varied at times, changing from pale pink to a deep red, but they retained their

From the Department of Dermatology, Northwestern University Medical School, Edward A. Oliver, chairman

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individual shapes for practically the entire period that the patient was under observation. During the periods of quiescence some of the lesions healed to the point that they could not be distinguished readily from neighboring normal areas. Usually the areas between the lesions seemed normal in appearance except during one acute phase when the entire tongue became swollen and red.

There was never any ulceration, bleeding or discharge from the lesions. The buccal mucous membranes and gingivae appeared healthy, and the teeth were in good condition. There was no regional adenopathy.

The general physical examination revealed normal findings except for a small erosion on the cervix. The hemogram, which was studied on numerous occasions over a period of six years, was always normal. Repeatedly the results of urinalysis were normal, and the serologic tests of the blood elicited negative reactions. The metabolic rate ranged at times from minus 2 per cent to plus 11 per cent. The studies of the blood chemistry showed normal amounts of proteins, albumin, globulin, cholesterol, calcium and phosphatase. The gastric analysis showed normal amounts of free hydrochloric acid and total acid. On examination, the feces were found to be free of tapeworm segments or ova. Allergy studies were made by means of percutaneous tests and diet elimination but contributed no pertinent information. The eosinophil count was normal. A thorough study by a psychiatrist revealed no findings to warrant a diagnosis of hysteria or self-induced lesions. There was no evident endocrinopathy, the department of stomatology and oral surgery had no suggestions to make with regard to further studies.

Histologic studies of sections of the tongue by Dr. Evangeline E. Stenhouse revealed changes indicative of superficial glossitis, acute and subacute in nature.

*"Center of Tongue"*—The epidermis is atrophic and shows only rudimentary papillae and interpapillary processes. There is a thickened, horny layer comprising about one half the thickness of the epithelium. There is a granular layer about 2 to 3 cells in thickness. The basal portion consists of cuboidal cells not arranged definitely in palisades. The tunica propria is involved in its entire thickness in subacute and chronic inflammation. There are many new-formed capillaries with swollen endothelium. In places there are a good many plasma cells. Beneath the tunica propria the superficial muscle fibers are involved in mild inflammation, and some of them have undergone hyaline degeneration.

*"Left Side of Tongue, Eroded Area"*—The section shows no epithelial covering. The superficial portion is composed of a fibrinous material containing round cells and polymorphonuclear cells. The entire tunica propria is involved in acute and subacute inflammatory change, with many polymorphonuclear cells in superficial blood vessels, the endothelial lining of which is swollen. The superficial muscle fibers are also involved, with hyaline change in a few of the fibers.

The patient received as treatment from various physicians large doses of mixed vitamins, cod liver oil, dried yeast, dilute hydrochloric acid, atropine and alpha-estradiol benzote (in sesame oil). Estrogenic substances were applied to the tongue and administered by mouth and parenterally. At one time 10,000 units of estrone in oil was administered five times weekly for two weeks, with the thought that such a dosage might produce bleeding from the tongue in the event that it contained aberrant endometrial tissue. Soothing preparations were prescribed for topical application to the tongue. With these measures the tongue would improve for a time, both subjectively and objectively, but there was never complete healing and new lesions would continue to make their appearance. Unfortunately, she was not treated with anhydrohydroxyprogesterone or corpus luteum substance. At the time of this writing the patient is again pregnant, and again, for the second time in a period of six years, the lesions and subjective symptoms have disappeared.

When this case was presented at the Chicago meeting Moeller's glossitis was the diagnosis favored by most of the members who discussed it, but the question was raised as to its nosologic position. Moeller's glossitis is a disease which seems to occupy an uncertain nosologic position. The literature on the subject is small (less than 100 cases have been recorded), and there are but few important papers on the subject. Dermatologic textbooks give it some attention, the literature of otolaryngology disregards it, and among the books on stomatology only that by Prinz and Greenbaum<sup>1</sup> gives it serious consideration. The subject has received most attention from German physicians, who consider it to be a definite clinical entity associated with pernicious anemia, but it receives only scant mention in the literature of hematology and internal medicine.

Moeller in 1851, under the title "Chronic Superficial Excoriations of the Tongue," was first to describe the disease, and his clinical description leaves little to be added.

Irregular, usually sharply defined vivid red spots from which the epithelium is missing or has become thinned. The papillae appear hyperemic and swollen and are elevated above the level of the normal mucous membrane. The areas are not covered with a pathological discharge, they are not transformed into ulcerations, nor do they have a tendency to spread. They are persistent, retaining their original size and form in spite of all forms of treatments. The lesions occur usually on the tip and margins of the tongue and sometimes the undersurface and inside of the lips. The excoriations cause a very annoying burning sensation giving a distaste for even the mildest of foods, although the appetite does not suffer. The sense of taste is dulled and sometimes the articulatory movements of the tongue cause pain.

Moeller reported and described 6 cases with similar symptoms in all of which the patients were women of middle age who had been troubled with the disease for many months.

Moeller's paper apparently aroused little attention in medical circles, for no further reports appeared in the literature until 1890—forty years later—when Michaelson reported 3 cases, 1 of them the case of a man, the first reported. Several scattered reports appeared thereafter in the German literature, none of which added materially to Moeller's original report except to increase the number of cases on record. The French and English ignored the disease, the French apparently confusing it with geographic tongue, "one form of which is accompanied with considerable subjective sensations while the edges are missing" (Bernard).<sup>2</sup> In 1909 the authoritative William Hunter contended that an early and invariable symptom of pernicious anemia was soreness of the tongue from glossitis. He described superficial ulcerations as more or less

1 Prinz, H., and Greenbaum, S. S. *Diseases of the Mouth and Their Treatment*, ed. 2, Philadelphia, Lea & Febiger, 1939.

2 Heyn, W. Moeller's Glossitis, Hunter's Tongue and Pernicious Anemia, *Dermat Ztschr* 47 132, 1926.

regular occurrences, but otherwise his description of the lesions was essentially similar to that of Moeller's glossitis, "fiery red patches, pain on eating, chronicity, periodicity and absent epithelium" Hunter focused attention on the connection of sore tongue with pernicious anemia, and the term "Hunter's glossitis" appeared for many years in the English and American literature of hematology and internal medicine. It is not yet clearly settled whether Hunter's glossitis and Moeller's glossitis are essentially the same disease, but they would seem not to be, because ulcers are a conspicuous part of Hunter's glossitis and they never occur in Moeller's description of the disease. Incidentally, today both terms are virtually ignored in all but the dermatologic literature.

In this country attention was first called to the condition by Fred Harris in 1915.<sup>3</sup> Like all other papers on the subject, Harris' paper was of a casuistic nature, but his report of 20 cases, 2 of them from his own practice was a thorough analytic study, covering every phase of the subject. From it he concluded that Moeller's glossitis was a distinct clinical entity of unknown cause and that, while it was undoubtedly uncommon, it probably was not so rare as the number of cases reported would lead one to judge. That position after thirty years may well be supported today, for the published transactions in journals of dermatology indicate that, although patients with the disease are only occasionally presented before the various dermatologic societies, the members who discuss them frequently refer to their experiences with other similar cases.

Schafer<sup>4</sup> then enlarged the clinical concept of Moeller's glossitis to include a latent form without the acute symptoms, a type in which there is burning only or, after the stage of burning, a condition of smooth atrophy with or without transparent swellings. Greenbaum noted that it is difficult to differentiate the latter condition from painful geographic tongue, though in their textbook he and Prinz did give recognition to Schafer's classification. Schafer stressed the connection between pernicious anemia and Moeller's glossitis. In fact, he maintained that the diagnosis of Moeller's glossitis can be entertained only if, in addition to the symptoms, there are also changes of the blood as in pernicious anemia.

In a comprehensive paper, Heyn<sup>2</sup> in 1926 reported on 37 cases observed in the years between 1920 and 1924. His group included 30 women and 7 men, and, as in Harris' study, Heyn gave a complete and thorough exposition of the subject, with particular attention given to the cause of Moeller's glossitis. He concluded from his cases that "Moeller's glossitis together with chronic intestinal disturbances, mostly achylia,

3 Harris, F. Chronic Superficial Excoriation of the Tongue, *J. Cutan. Dis.* 33: 742, 1915.

4 Schäfer, E. A Contribution to the Knowledge of Moeller's Glossitis and Its Relation to Pernicious Anemia, *Arch. f. Dermat. u. Syph.* 147: 201, 1924.

may be symptoms of a number of diversified diseases, the outcome of which may be pernicious anemia. Moeller's glossitis often is a forerunner of pernicious anemia." He found pernicious anemia in 75 per cent of his cases, and in 21 per cent there were findings to warrant suspicion of pernicious anemia. He found no examples of Moeller's glossitis in patients with other types of anemia. With regard to Schafer's classification, Heyn conceded that formes frustes probably do occur, but they cannot be recognized, for they hardly cause the patient to seek medical aid.

Zinsser,<sup>5</sup> as well as most of the German school of physicians, considered Moeller's glossitis to be a manifestation of pernicious anemia, but in this country the connection between Moeller's glossitis and pernicious anemia has not been noted by Harris, Fred Wise, Oimsby, Rostenberg, Cole, Engman, Stillians and others who have observed cases of the disease. In the case herein reported there is no indication of pernicious anemia. Greenbaum, however, who has studied the subject extensively, did consider it to be a manifestation of pernicious anemia.

From time to time other causative factors have been suggested. Of Moeller's 6 patients, 2 had gastroenteritis, 2 had anemia and 5 were affected with fish tapeworm, a factor to which Moeller attached significance, but his paper appeared in 1851, only two years after Addison's historic description of pernicious anemia was published and twenty years before Biermer established the concept of pernicious anemia in German medicine. The causative role of tapeworm has been mentioned in several cases either as a direct cause or as an indirect cause, for it was once thought that tapeworm caused pernicious anemia. Sturgis and Isaacs, however, dismissed this suggestion on the grounds that pernicious anemia is relatively rare in persons with tapeworm, that in such persons treatment with liver substance has effected recovery from pernicious anemia before the tapeworm was expelled and relapses of the pernicious anemia have occurred after the tapeworm had been expelled.

It has been suggested that Moeller's glossitis is a nonspecific entity that may accompany almost any type of anemia or dyscrasia, but the literature of hematology does not support that view. A reflex neurosis, particularly from gastroenteritis, was credited with causing Moeller's glossitis, but that theory, too, has been dismissed. Engman and Weiss<sup>6</sup> have reported a case of Moeller's glossitis which was cured after the extraction of abscessed teeth and the eradication of pyorrhea in a woman.

5 Zinsser, F, in Jadassohn, J. *Handbuch der Haut- und Geschlechtskrankheiten*, Berlin, Julius Springer, 1930, vol 14, p 1.

6 Engman, M. "Burning Tongue," *Arch Dermat & Syph* 1 137 (Feb) 1920.

The influence of hormonal factors on Moeller's glossitis has been suggested frequently, because most of the patients have been women, in many of whom the onset coincided with the onset of menopause. In Heyn's series "some women claimed the tongue was worse during the menstrual period" one patient observed a remission during menstruation."

In the case herein reported the patient was younger than those in other recorded cases. The lesions were more inflammatory and painful during the menstrual period, and there was complete remission of symptoms during two pregnancies, an observation that apparently has never before been recorded.

#### SYMPTOMS AND DIAGNOSIS

The most important symptom of Moeller's glossitis and the one that causes the patient to seek medical aid is the intense burning pain of the tongue. The burning might begin suddenly, in which case the patient usually associates it with some specific occurrence, as a nervous shock, dentistry or a gastric upset, but usually the onset is gradual. The early writers stressed the constancy and severity of the pain and described it as being aggravated by highly seasoned foods and to the extent that each intake of food was a torture. Yet there seems to be no complaint of loss of appetite though the sense of taste may be dulled. As more cases were observed, it became evident that the subjective complaints might be variable, some patients describing the sensation as itching rather than burning or characterizing it as mere discomfort or insignificant. The burning sensation may sometimes radiate to the ear, or it may be present in the throat and esophagus. According to Heyn, the pain may even disappear completely for weeks or months. Nevertheless, pain is the outstanding symptom of Moeller's glossitis, and it is difficult to make a diagnosis of Moeller's glossitis unless the patient does complain of pain.

The burning sensation does not involve the entire tongue, rather it is confined to the patches of glossitis which are usually situated on the tip and lateral margins of the tongue. In a typical case the lesions are readily recognized, for they are sharply outlined and of vivid red color and the covering epithelium is so thinned that the patches at first glance appear to be excoriated. They occur usually as irregular round or oval patches, but they may be elongated or streaked with ragged or arciform borders which make them look somewhat like factitious lesions. The individual lesions may be small, the size of a lentil, but oftener they attain the size of 1 or 2 cm. Characteristically, they retain their original size and configuration, showing but little tendency to spread or coalesce. The patches are not infiltrated. The lesions feel somewhat softened or flabby and are slightly depressed rather than elevated. The papillae within the patches, however, may be hyperemic, swollen and elevated above the level of the surrounding surface and

they may be exceedingly tender to touch. Some observers consider this papillitis to be an essential part of the picture of Moeller's glossitis.

The mucous membrane between the patches appears to be either normal or slightly edematous and shiny gray. The consistency of the tongue remains practically normal, but when the tongue is extended whitish longitudinal streaks appear on the dorsum near the base of the tongue. These streaks change their direction during movements of the tongue from side to side, and, according to Arndt, who first called attention to these changes, the streaks are probably due to increase of pressure of subsurface inflammation of the tissue and they constitute a sign of diagnostic significance, especially during stages of remission.

In Moeller's glossitis there are characteristically no ulcers, fissures, erosions or scales, there is no peeling or discharge from the lesions, the tongue is usually not coated, and no scarring results from the lesions.

#### DIFFERENTIAL DIAGNOSIS

Other diseases of the tongue that are characterized by patches or pain may closely simulate Moeller's glossitis. The disease which apparently causes most confusion is the entity "transitory benign plaques of the tongue" (also called wandering rash, geographic tongue, erythema migrans, exfoliative areata linguae and other names), especially the cases in which the lesions are painful. In this disease the lesions do not retain their original size or shape, they begin usually as pea-sized lesions and enlarge by peripheral extension to circular or oval rings  $\frac{1}{2}$  inch (1.2 cm) wide or larger. The borders have a yellowish tint, and they are slightly raised so that the circles are visible at a distance. Neighboring lesions have a tendency to coalesce to form gyrate figures. The lesions are evanescent. Pain, tenderness and chronicity, although they may occur occasionally, are not prominent features of the disease. Thus the disease can be readily distinguished from Moeller's glossitis except on a rare occasion such as Stillians has experienced, in which a patient apparently had lesions of both Moeller's glossitis and geographic tongue.

The various lesions of syphilis, particularly the mucous patches, patchy stomatitis medicamentosa, erythema multiforme and perhaps pemphigus and epidermolysis bullosa must also be differentiated from Moeller's glossitis. Factitious lesions may sometimes simulate Moeller's glossitis. Feigned eruptions are exceedingly rare in the mouth. Such lesions should have bizarre shapes with streaks and angulations, and the subjective sensations of pain and burning are apt to be greatly exaggerated, particularly when the tongue is being examined by the physician. At one time or another, however, it is usually possible to distract the patient during an examination.

Mucous patches of syphilis exhibit little or no soreness. They are round or oval, flat, slightly depressed or, rarely, barely elevated above

the surrounding parts. The surface of a patch has a pale rose or gray color, and it is moistened with mucus. The mottled tongue in late syphilis or the smooth, shiny, varnish-like lesions due to syphilitic sclerosis of the deeper tissues of the tongue may also be readily distinguished from Moeller's glossitis by the presence of infiltration in the lesions and the absence of pain.

In stomatitis medicamentosa, erythema multiforme and other bullous diseases affecting the mouth, the patches are eroded and partially covered by loosely attached grayish white shreds resembling milk curds.

The various diseases that produce pain and burning of the tongue must also be distinguished from Moeller's glossitis. When pain is due to organic lesions as tuberculosis, aphthous lesions, herpes or stomatitis venenata, clinical pictures of those diseases are usually familiar and readily recognized.

More difficulty from the standpoint of differential diagnosis is presented by the conditions in which there is pain or burning but no obvious changes in the tongue, a condition which exists, according to German physicians, in Moeller's glossitis during periods of relative remission.

Such symptoms may have a psychic origin, occurring as a manifestation of hysteria or more commonly in person with cancerphobia, as Engman<sup>6</sup> has pointed out. Glossodynia has been noted in aphasic disorders, in peptic ulcer of the stomach, as a nervous manifestation, as a reflex irritation from malocclusion of the temporomandibular joint, in glossopharyngeal neuralgia, as a manifestation of allergy to foods, drugs, dentifrices and materials in dental plates, in arteriosclerosis of the vessels of the tongue, in patients with artificial replacements in the upper jaw, as a manifestation of lingual tonsillitis, and in pellagra, sprue and related conditions in which there is avitaminosis or dysvitaminosis. Burning tongue with or without visible stomatitis is occasionally due to galvanism from dissimilar metals in teeth. In such cases the patients usually note that the onset followed soon after dentistry was performed, and they complain not only of the burning sensation but also of a peculiar metallic or salty taste in the mouth, sometimes a dry tickling feeling in the throat and an increased amount of salivation. The symptoms are usually relieved by eating or drinking rather than aggravated as in Moeller's glossitis.

Burning and painful tongue occurs oftener as a result of anemias perhaps than from any of the aforementioned conditions. Yet there is seemingly a difference of opinion among hematologists as to the importance or frequency of glossitis in patients with anemia. Sturgis and Isaacs, who wrote the chapter on pernicious anemia in Downey's encyclopedic "*Handbook of Hematology*,"<sup>7</sup> merely stated, "The common gastrointestinal symptoms [of pernicious anemia] are recurrent attacks

7 Downey H. *Handbook of Hematology*, New York, Paul B. Hoeber, 1938.

of glossitis " and there is no description of the tongue Wintrobe<sup>8</sup> stated, "in pernicious anemia glossitis and atrophy of the tongue papillae are common" Murphy commented that in pernicious anemia "early the edges or surface of the tongue may be inflamed with a bright scarlet hue later, [there is] glossitis with the smooth, shiny, rather opalescent sheen" And of idiopathic hypochromic anemia he stated that soreness of the tongue is sometimes complained of but inflammation or true glossitis, if it occurs, must be extremely rare However, Dameshek<sup>9</sup> was not in agreement, for he observed that primary hypochromic anemia is always characterized by an abnormal tongue, which early is intensely red and later becomes atrophied, shiny and bald The involvement is usually of the entire dorsum of the tongue, but at times only small areas of redness are present on the tip of the tongue Whitby and Britton<sup>10</sup> also stated that in idiopathic hypochromic anemia "rarely the mouth affection may be severe, with much redness and extreme pain there may be shallow ulcers The glossitis may progress to produce a smooth, red, bald tongue, pale and atrophic The glazed tongue is more constant in this condition than in pernicious anemia" Similar changes were attributed by McCombs<sup>11</sup> to deficiency of nicotinic acid, while Hutter, Middleton and Steenbock<sup>12</sup> pointed out that the glossitis of pregnancy, pellagra, sprue, Plummer-Vinson syndrome, malnutrition, intestinal stricture and the various anemias have one thing in common vitamin B deficiency and in all these diseases there occurs stomatitis

## COMMENT

There is thus a difference of opinion as to whether or not Moeller's glossitis constitutes a disease entity, whether or not it is a manifestation of pernicious anemia and whether it is characterized by a distinctive clinical picture Sutton and Sutton,<sup>13</sup> for instance, considered that it falls into four classes stomatitis venenata, stomatitis due to systemic allergy, stomatitis due to nutritional deficiency and glossodynia European physicians, particularly the German school, have considered it to be a manifestation of pernicious anemia Physicians in this country in general have not noted that connection, and it is significant that the literature on hematology, which has grown to voluminous proportions in recent

8 Wintrobe, M M Clinical Hematology, Philadelphia, Lea & Febiger, 1942

9 Dameshek, W Primary Hypochromic Anemia, J A M A **100**:540 (Feb 25) 1933

10 Whitby, L E, and Britton, C J Disorders of the Blood, ed 3, Philadelphia, The Blakiston Company, 1939

11 McCombs, R B Internal Medicine in General Practice, Philadelphia, W B Saunders Company, 1943

12 Hutter, A M, Middleton, W S, and Steenbock, H Vitamin B Deficiency and the Atrophic Tongue, J A M A **101** 1305 (Oct 21) 1933

13 Sutton, R L, and Sutton, R L, Jr Introduction to Dermatology, ed 4, St Louis, C V Mosby Company, 1941

years, pays but scant attention to Moeller's glossitis. The literature would seem to indicate, too, that the complaint of painful burning tongue, though not uncommon, is not a prominent symptom of anemia. Pernicious anemia is not uncommon, painful burning tongue sufficient for the patient to seek medical aid is relatively rare. Pernicious anemia usually can be influenced by treatment, Moeller's glossitis is affected but little by treatment. It would seem, therefore, that Moeller's glossitis is not necessarily a manifestation of pernicious anemia unless one is prepared to accept the concept that glossitis may be a forerunner of the changes in the blood. The case herein reported has been observed for six years, and repeated examinations of the blood over a long period have failed to reveal any evidence of pernicious anemia.

There is a difference of opinion, too, as to what constitutes the clinical picture of Moeller's glossitis, but if Moeller's description is to be accepted—as it should be—the morphologic changes and subjective symptoms are so sharp that they could hardly be missed. Yet the type of glossitis that is described as part of the picture of anemia is not similar to the glossitis that Moeller described. It would seem unwise, too, to enlarge the concept of the clinical picture into latent and florid forms, a type in which there is burning only or a form with smooth atrophy, for Moeller and most of the early writers have stressed as important symptoms the presence of persistent painful, red areas which do not respond to treatment, and their patients did not exhibit atrophy of the tongue.

The obvious conclusions to be drawn are no different from those made by Harris thirty years ago that Moeller's glossitis is a distinct type of inflammation of the tongue the cause of which is not known.

#### SUMMARY

A case of Moeller's glossitis in a young woman is reported. It has been present constantly for six years except on two occasions when she was pregnant. Complete remission of the disease during pregnancy has apparently never before been recorded.

The characteristics are listed which distinguish Moeller's glossitis from other diseases which produce areas of glossitis and from those in which there is burning and painful tongue.

Moeller's glossitis constitutes a distinct clinical entity, which, though uncommon, is probably not so rare as the scarcity of recorded cases would indicate. Its cause is not known, and, though in most cases it is said to occur in association with pernicious anemia, the connection cannot always be demonstrated. In the case herein reported there were no signs of anemia, there was a decided hormonal factor.

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#### ABSTRACT OF DISCUSSION

DR EDWARD A. OLIVER, Chicago. Dr. Rattner has given us a most interesting and comprehensive discussion of this little known disease, known as Moeller's

glossitis I have personally seen and examined this patient several times with him, and his description is an accurate one

It was only after much consideration that we came to that diagnosis. The disease is not common, nor is it rare. We in Chicago have always been aware of it, chiefly because of the interest of our fellow Chicagoan, Fred Harris, in it. He called it to our attention in 1915. Since that time, we have been constantly on the lookout for it in rather obscure cases of painful tongue, and Dr. Senear and I have seen probably 2 cases of it in a number of years.

The serious feature of the disease is the exquisite pain and burning of the individual patches. The pain and sensitiveness may be compared with those produced by a second degree burn. Changes of temperature, contact with food, acid, salt and other condiments and even contact with the teeth and gums produce exquisite pain.

In this case, as in all others that have been described or in the cases that we have seen, there has been no associated pernicious anemia, nor has there been any associated avitaminosis. The fact that in this case the patient has been entirely well during her pregnancies points to a hormonal factor, and the fact that in Moeller's original report the patients were all women of middle age lends substance to that view. Dr. Rattner has explored that and all other fields to the utmost without discovering the cause of this most unusual case, and it is hoped that some time in the future a definite causal factor will be discovered for Moeller's glossitis.

DR FRANCIS E. SENEAR, Chicago. I think that we are indebted to Dr. Rattner for calling attention to this subject. As happens often in dermatology, we become locally interested in a disease through a report such as that of Fred Harris in Chicago. I know that I presented a case before the Chicago Dermatological Society in the past year or two and found that even there, where the disease had been fathered in this country, we had so much lost track of it that many of the young men had never heard of Moeller's glossitis. As Dr. Oliver said, we have seen 2 cases together and I have seen 3 more at the University of Illinois College of Dentistry, making a total of 5 that I have in mind.

I had the privilege of seeing 1 of Fred Harris' 2 original cases, and later on he saw with me the man in the group of patients whom I have seen. That patient was in the later age group, so, as some one said in the discussion of Dr. Callaway's paper, he might well have come within the male climacteric period, and one could well believe, if there is a hormonal background for this disease, that his condition may have had such a background.

I have been much interested in disease of the mucous membranes for a long time, because a course is given to dentists each year in the University of Illinois College of Dentistry and these cases have been followed closely. I feel that there are two things that can be said, both of which Dr. Rattner has already brought out: first, that there is no connection with pernicious anemia on the basis of our experience, these patients have all been studied carefully, with no suggestion of anemia found in any of them, and, second, that the clinical characteristic is so definite that one feels that clinically there is such a thing as Moeller's glossitis. The sharp circumscription of the patches and the excessively raw, bright red appearance make it unlike any other disorder of the mucous membranes with which I am familiar, and certainly I do not think that there would be any difficulty ever, even with the atypical cases of geographic tongue, in differentiating them clinically.

# TUBERCULOID LEPROSY OF LUPOID APPEARANCE

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WE THOUGHT this case worthy of being reported because of the resemblance of the lesions to lupus tumidus nonexedens and lupus tumidus exedens psoriasiformis. The clinical likeness was almost exact except that the lesions of true tuberculous lupus are easily perforated with a probe. It is also noteworthy that the evolution of the disease was of long duration but that there was never any phase of reaction.

## REPORT OF A CASE

E M, aged 22, a single Brazilian woman, not of the white race, a domestic servant, was living at Curvelo in the state of Minas Geraes.

There was no history of the patient having lived among lepers.

The patient stated that six years previously a lesion appeared on the middle of the upper third of the outer surface of the right forearm, this lesion increased in size until it attained its present dimensions. At the same time other lesions appeared at the level of the right maxillary region.

A general examination showed nothing abnormal.

A dermatologic examination showed that the lesions were situated at three different sites, namely the face, the right arm and the right forearm. The facial lesion was at the level of the right mandibular angle and consisted of nodules varying from 0.5 to 1 cm in diameter. These nodules were clustered together in vaguely arched patches. The disease had lasted for six years (fig 1).

The patch of skin included in the arched grouping was slightly atrophied. The color of the skin was normal both at the center of the lesion and at the periphery. The lesions were yellowish red and on palpation were succulent and easily compressed by the fingers. The skin covering the lesions was smooth, shining and slightly squamous. On pressure with glass a bistere-colored tissue was observed. The other lesion was situated at the level of the right elbow, covering the upper half of the posterior surface of the right forearm and the epitrochlear region and extending to all the anterointernal surface of the elbow joint. At this point the dermatosis consisted of two extensive plaques. The oleocranial region was not affected. The first plaque, that on the forearm, was about 15 cm long and 8 cm wide. On examining any of the lesions with the curet, one saw that they were not friable but easily depressible. The lesion consisted of various tuberculous groups of the same color, aspect and consistency as those on the face. In the groups of lesions, isolated nodules could be seen here and there, the skin between them was either normal or atrophied, with slight follicular pigmentation. Some lesions were ulcerated and covered with dark-colored crusts. The lesion on the inner

surface of the elbow was 10 cm long and 6 cm broad. The areas of healthy skin at this site were much smaller, the nodules were grouped in one extensive, more or less uniform plaque (fig 2). The lesions showed longitudinal folds, which were in conformity with their relative flaccidity. This plaque, like the first one



Fig 1—Tuberculoid leprosy of lupoid appearance, like lupus tumidus non-exedens



Fig 2—Tuberculoid leprosy of lupoid appearance, like lupus tumidus exedens psoriasiformis

described, was copper red and squamous. The lesions showed a certain translucence, allowing a fine arborization of blood vessels to be seen. When the sensibility was tested, superficial tactile hypesthesia was noted, with conservation of sensibility

to pain and heat. Nothing special was noted in the nerves which could be reached for examination. The eruption should be differentiated from common lupus, lupoid sporotrichosis, Boeck-Schaumann sarcoid and nodular syphilid.

A roentgen examination of the mediastinum, lungs and phalanges showed nothing abnormal.

A search revealed no alcohol-resistant or acid-resistant bacilli in the lesions. An inoculation of a guinea pig with material from the lesions produced no reaction (thirty days later). The Mitsuda reaction was tardily positive, with the peculiarity that the aspect of the patient's nodules was faithfully reproduced (an isomorphic reaction).

Tuberculin in dilutions from 1:100 to 1:1,000,000 elicited negative reactions.

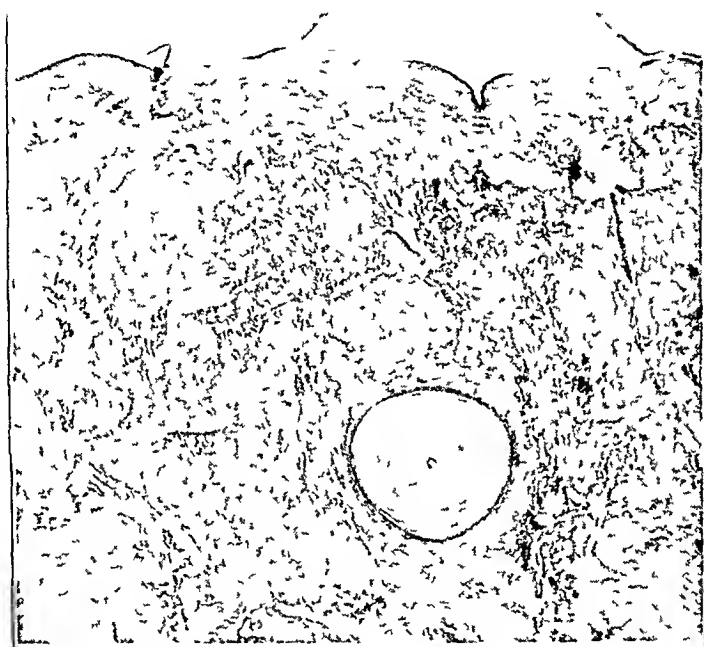


Fig. 3—Tuberculoid leprosy of lupoid appearance. General view of the lesion.

A histologic examination was carried out by Dr. Moacyr A. Junqueira, who gave the following report:

The fragment for examination was taken from the lesion on the forearm. There was keratosis, the corneal layers separating easily; a small area of parakeratosis was noted. The granular layer and the rete were atrophied. The basal layer was slightly sinuous and almost horizontal and showed areas of depigmentation. In two follicular orifices included in the section, dilatation and hyperkeratosis were noted. The derma was filled throughout with a dense inflammatory infiltrate, consisting of granulomas which at times ran together to form extensive areas. This infiltrate entered into contact with the epidermis at various points, causing it to atrophy through compression. These granulomas consisted of epithelioid cells, with a few giant Langhans cells and large numbers of lymphocytes at the periphery. In only one of these granulomas was there found a small area of fibrinoid necrosis at the center. Two horny cysts were seen in the tuberculoid infiltrate; one of these cysts corresponded to one of the follicles already mentioned.

Granulomas were found even in the superficial layers of the hypoderm. The vessels in the hypoderm and in the neighborhood of the dense and extensive infiltrate were, as a rule, dilated and surrounded by a lymphocytic sheath. In preparations stained by the Ziehl-Neelsen method, no alcohol-resisting or acid resisting bacilli were found (fig 3).

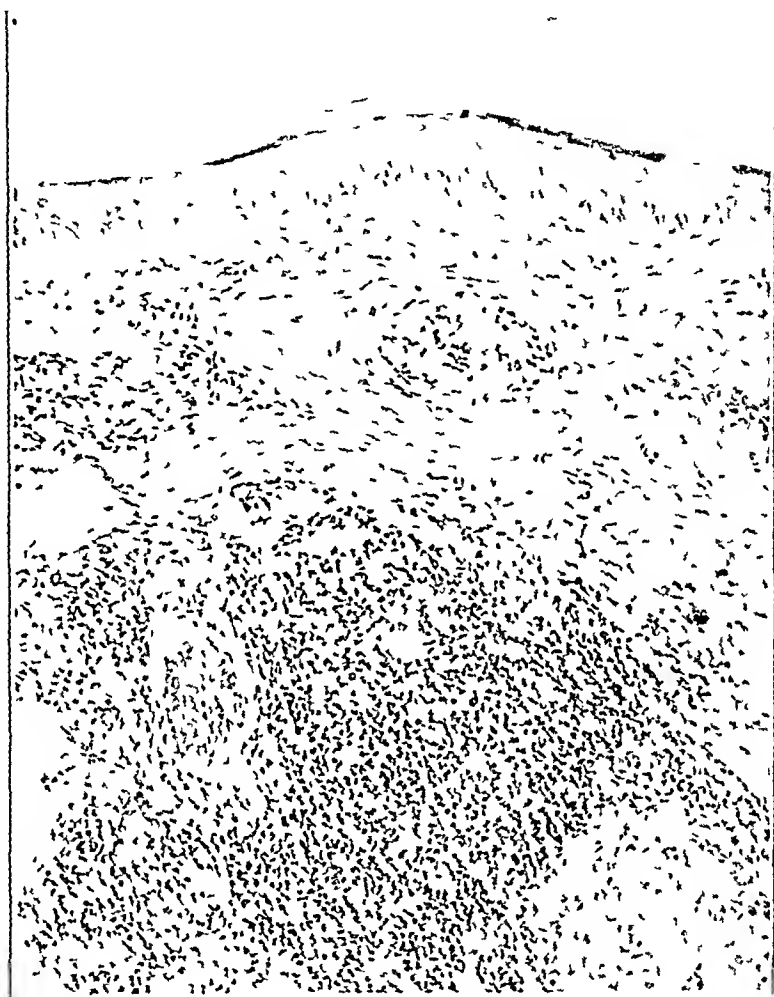


FIG 4—Tuberculoid leprosy of lupoid appearance. Details of the preceding figure. Note the abundance of lymphocytes in the periphery of the tuberculoid nodules.

#### SUMMARY

We have described a case of tuberculoid leprosy which we believe is interesting for (1) the extraordinary likeness of the lesions to lupus tumidus nonexedens and lupus tumidus exedens psoriasiformis, (2) the long evolution of the disease without any manifestation of other lesions except the original ones, and (3) the nodules resulting from the Mitsuda-Rost test with their exact similarity to the nodules already described (isomorphic reaction).

Rua Ceará, 1691

# RETICULUM, OR LATTICE, FIBERS

Further Studies

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THESE studies pertaining to the argyrophil, reticulum or lattice fibers had a threefold purpose, first, to inquire into the factor or factors responsible for their development, second, to account for their presence in areas distant from vessels and infiltrating cells and, third, to inquire into their function and diagnostic value. In view of the scant attention that has been paid to the subject in dermatologic circles, it appears justifiable to begin with the fundamentals, even at the risk of approaching the elementary. Regardless of the voluminous literature, the histogenesis of these fibers is still a debatable problem.

Ormsby and Montgomery<sup>1</sup> hinted at their importance when they stated that "there is a third system of fibers in the corium known as reticulum or lattice fibers which increase in numbers in various pathologic conditions, especially those involving the reticulo-endothelial system of the skin."

Oppel<sup>2</sup> in 1891 seems to have been the first to use the term "lattice fibers" in describing the peculiar formations of connective tissue discovered by Kupffer which were present between the hepatic cells. Mall,<sup>3</sup> in the same year, announced that the framework of many organs and other tissues of the mammalian body is composed neither of white fibrous nor of yellow elastic connective tissue but of a third type of supporting substance, consisting of fine, interlacing fibrils which not only differ from the white fibers in appearance but are more resistant to both acid and alkaline solvents and are not as readily attacked by digestive ferments. To this new tissue, the word "reticulum" was applied because the fibrils of the lymph nodes, already bearing that name, were the first which he found to present the characteristics just men-

Read at the Sixty-Sixth Annual Meeting of the American Dermatologic Association, Hot Springs, Va., June 10, 1946

1 Ormsby, O. S., and Montgomery, H. M. *Diseases of the Skin*, Philadelphia, Lea & Febiger, 1943, p. 18

2 Oppel, A. *Ueber Gitterfasern der menschlichen Leber und Milz*, *Anat Anz* 6:165, 1891

3 Mall, F. P. *Das reticulirte Gewebe und seine Beziehungen zu den Bindegewebsfibrillen*, *Abhandl. d. math.-phys. Cl. d. k. sachs. Gesellsch. d. Wissensch.* 17:299, 1891

tioned In its present day usage, reticulum is a term applied to the form of connective tissue which is stained by silver impregnation methods Mall's paper also demonstrated that the supporting fibrils of the spleen, gastric and intestinal mucosae, liver, lung, thyroid, cardiac muscle, basement membrane of the testes and the entire supporting structure of the kidney, including the basement membranes, were of the same type

Maresch<sup>4</sup> in 1905, besides demonstrating lattice fibers in the liver and lymph nodes, showed that the musculature of the gravid uterus contains similar supporting structures As to the skin, Ferguson<sup>5</sup> in 1911 appears to have been the first to mention their presence, at the dermoepidermal juncture Zurhelle<sup>6</sup> in 1921 observed lattice fibers in the lymph nodes while investigating the pathologic changes occurring during the primary and secondary stages of syphilis and in a later study described their presence in numerous diseases of the skin Later, Way and Klovekorn,<sup>7</sup> in 1926, while working in E Hoffmann's clinic, under the direction of Zurhelle, studied the relationship of lattice fibers to normal and abnormal dermal structures and investigated eighty different dermatoses The present paper repeats in part some of the earlier findings, for the benefit of English readers, and includes additional observations

#### ORIGIN AND SIGNIFICANCE

Maximow and Bloom<sup>8</sup> stated that "Two main theories have been developed According to the first, fibers develop through a direct transformation of living substance of the cells According to the second theory, they arise between the cells through a condensation or crystallization of the liquid or semiliquid intercellular substance secreted by the cells Some authors believed in a direct transformation of the cell processes of the fibroblasts into collagenous fibers, while others thought that they originate from mitochondria arranged longitudinally at the cell surface, which then separate from the cytoplasm"

4 Maresch, R Ueber Gitterfasern der Leber und die Verwendbarkeit der Methode Bielschowskys zur Darstellung feinsten Bindegewebsfibrillen, *Centralbl f allg Path u path Anat* **16**:641, 1905

5 Ferguson, J S The Reticulum of Lymphatic Glands, *Anat Rec* **5**:249, 1911

6 Zurhelle, E Histopathologische Studien an syphilitischen Lymphdrüsen des primären und sekundären Stadiums, *Dermat Ztschr* **34** 1, 1921 Derselbe Ueber den anteil feinsten Bindegewebsfibrillen, der sogenannten Gitterfasern, am Aufbau syphilitischer und anderer Hautefflorenzen, gleichzeitig ein Beitrag zu ihrer Konsistenz, insbesondere zu Härte des Primäraffektes, *ibid* **35** 251, 1922

7 Way, S C, and Klovekorn, G H Hautkrankheiten und Gitterfasern, *Dermat Ztschr* **48** 139, 1926

8 Maximow, A A, and Bloom, W A A Textbook of Histology, ed 3, Philadelphia, W B Saunders Company, 1938, p 98

Corner,<sup>9</sup> in discussing the origin of reticulum, stated that "It seems certain endothelial phagocytes perform phagocytic functions, lay down fibrils of reticulum and collagen and transform themselves into giant cells or syncytia under pathologic conditions. Probably the entire endothelium, considered in the freest sense of the term, presents a persisting mesenchymal, embryonoid tissue capable of extensive differentiation or de-differentiation, without which the body would be incapable of repairing the ravages of disease and injury." He then concluded that, in view of the almost universal association of vascular endothelium and reticulin, a reticulum is produced regularly by this tissue. Furthermore, he has always been able to demonstrate capillaries in close proximity to reticular complexes, with one exception, fibroblasts appear to be capable of producing reticulin under certain conditions, particularly in the medullary rays of the kidney.

Regardless of the fact that the majority of authorities are in accord that the reticulum is produced either immediately or indirectly by certain reticuloendothelial cells, other investigators, especially Isaacs,<sup>10</sup> have taken exception and voiced the opinion that the fibrillar structures of the connective tissue are the result of the coagulating and dehydrating effect of chemical reagents and that collagenous tissue is composed of a homogeneous colloidal substance. Others claim that reticulocytes themselves may enter into the formation of reticular fibers, because they can be stained to show a skein or network of basophilic material. Similar consideration has been given also to the wandering cells of Marchand, which refers to certain sparse rounded cells of rough outline which circulate freely through the connective tissue lacunae. They have ameboid movements and have been considered endothelial leukocytes or emigrant lymphocytes from the blood.

Reticuloendothelial is a term which implies, according to Sachs,<sup>11</sup> an intimate relationship between the reticulum cells and the endothelial cells of such organs as the liver and lymph nodes in which the endothelial cells not only serve as linings of the blood and lymph sinuses but are also believed by some to produce reticulum fibers. If we employ the term reticulo-endothelial cells without implying that these two cell types are identical, there remains no valid reason why the term should not be acceptable for the collection of these cells in the spleen, liver, bone marrow and lymph nodes. The reticulo-endothelial system is also supposed to embrace the entire group of tissue mononuclear phagocytes.

The reticulo-endothelial system would thus consist of the reticulo-endothelial cells, that is, the reticular and endothelial cells of the spleen, liver, bone marrow, lymph nodes, adrenal and hypophyseal capillaries and the histiocytes (clasmatoocytes).

9 Corner, G. W. On the Widespread Occurrence of Reticular Fibrils Produced by Capillary Endothelium, *Contrib Embryol* 9 8, 1920.

10 Isaacs, R. The Structure and Mechanics of Developing Connective Tissue, *Anat Rec* 17 243, 1919.

11 Sachs, B. The Reticulo-Endothelial System, *Physiol Rev* 6 504, 1926.

and monocytes) of the tissues and the circulating blood. Whereas the term reticulo-endothelial cells would serve as a collective name for these elements, the terms reticular cells, endothelial cells, histiocytes, monocytes and clasmatocytes could be used to designate the individual elements where further differentiation is possible.

This reticuloendothelial concept also extends to the circulating blood.

Thus, Maximow and Bloom,<sup>12</sup> in discussing the origin of the blood cells, stated that

the cells of the circulating blood may be divided into two groups according to their origin in the hemopoietic tissues. To the first group belong the lymphocytes and probably monocytes. They originate in the lymphatic tissue and are called the lymphoid elements. The second group consists of the erythrocytes and the granular leukocytes. These originate in the myeloid tissue and are the myeloid elements. All of the blood forming tissues of adult mammals have the same fundamental structure, a fibrous and cellular stroma of reticular fibers and cells within whose meshes hemopoiesis takes place.

In the adult organism, the cells of the circulating blood seem to be quite independent from the connective tissue, but in reality, the relations between the two types are so intimate that no distinct line can be drawn between them. This is quite obvious if we follow the embryonic histogenesis of blood and connective tissue. It also becomes apparent under pathologic conditions especially in inflammation and in tissue cultures.

For the sake of completeness, the remaining constituents of the connective tissue of the skin will be briefly stated. The collagenous fibers are believed to be held together by a cementing substance that also forms a thin membrane on the surface of the fibers. The collagenous fibers, although nonelastic in the common sense of the word, are extremely flexible and offer great resistance to stress or strain. The elastic fibers branch at various angles and anastomose to form a more or less continuous network.

Many of the dermal structures, especially the cells, are believed to elaborate a jelly-like, amorphous substance which is related to the cement substance, keeping the fibrils together in the fibers and known as the "amorphous ground substance." These several kinds of connective tissues are probably much underrated. They play an important role in the nutrition of various elements embedded in them. Although this role is not completely understood, it is evident that all the substances which the cells of the other tissues receive from the blood and all the products of metabolism turned over to the blood and lymph must pass through some layer of connective tissue. There is also reason to believe that these products enter into the formation of reticulum fibers under normal and pathologic conditions and the investigations of Urbach<sup>13</sup> create the impression that they are also a factor in the mechanism of immunity.

<sup>12</sup> Maximow and Bloom,<sup>8</sup> p. 70.

<sup>13</sup> Urbach, E. *Textbook on Allergy*, New York, Grune & Stratton, Inc., 1943, p. 168.

Weidman<sup>14</sup> stressed the need for further studies regarding the origin of reticulum, or lattice, fibers because he has observed on numerous occasions the presence of dense networks of reticulum in areas distant from blood vessels and cellular infiltration

*Results of Studies of Seventy-One Tissues*

No of Cases	Name of Tissue	Location	Density of Lattice Fibers
1	Actinomycosis	Neck	+++
1	Acanthosis nigricans	Axilla	++
2	Amyloidosis of the skin	Leg	—
1	Angiosarcoma	Cheek	+
1	Apocrine glands	Axilla	—
4	Basal cell carcinoma	Nose, ear and back	+++
2	Blue nevus		++ and —
1	Carcinomatosis	Generalized	+++
1	Colloid milium	Hand	++
1	Eczema (pre-malignant)	Breast	+++
2	Fibroma	Wrist and arm	+ and —
2	Fibrosarcoma	Anus and ear	++ and —
2	Fetal skin (8 and 5½ mo)	Arm and leg	—
1	Glomus tumor	Forearm	+
1	Glossitis mediana rhombica	Tongue	—
1	Granuloma annulare	Hand	+
1	Granuloma pyogenicum	Gum	+
3	Leiomyoma	Finger and arm	—
1	Lichen planus	Back	+
1	Lipoma		—
3	Liver	Adult	+++
3	Lymph node	Adult	+++
1	Lymph node	Fetus	+++
1	Lymphosarcoma	Arm	+++
3	Melanoma	Ankle, foot and arm	+++
1	Mycosis fungoides	Neck	+
1	Myxedema	Ankle	—
3	Nevus verrucosus		—
6	Nevus pigmentosus	Ear and face	++ and —
1	Nevus pigmentosus (acanthotic type)		—
1	Radium atrophy	Forehead	++
2	Rhinoscleroma	Nose	++
1	Sarcoma (giant cell)		++
6	Sarcoma (squamous cell)	Lip and cheek	+++
1	Scleroderma	Back	—
1	Sebaceous nevus (colloid degeneration)	Cheek	++
3	Spleen	Adult	+++
1	Spleen	Fetus	+++
1	Syphilis	Chest	+++
1	Xanthoma tuberosum multiplex	Buttocks	+

MY STUDIES

For investigative purpose, seventy-one different tissues, normal and pathologic, were selected. In as far as possible, more than one example of a dermatosis was studied. Sections from each case were stained by

14 Weidman F D Personal communication to the author

the Maresch modification of the Bielschowsky method, Foot's modification of the Bielschowsky method, iron-hematoxylin and iodine-eosin, Weigert's stain for elastic fibers and Unna's orcein method for elastic fibers. As suggested by E. Hoffman, Van Gieson's and iron-hematoxylin methods were used as counterstains in both of the silver impregnation methods to demonstrate normal collagen and the reticulo-endothelial cells.

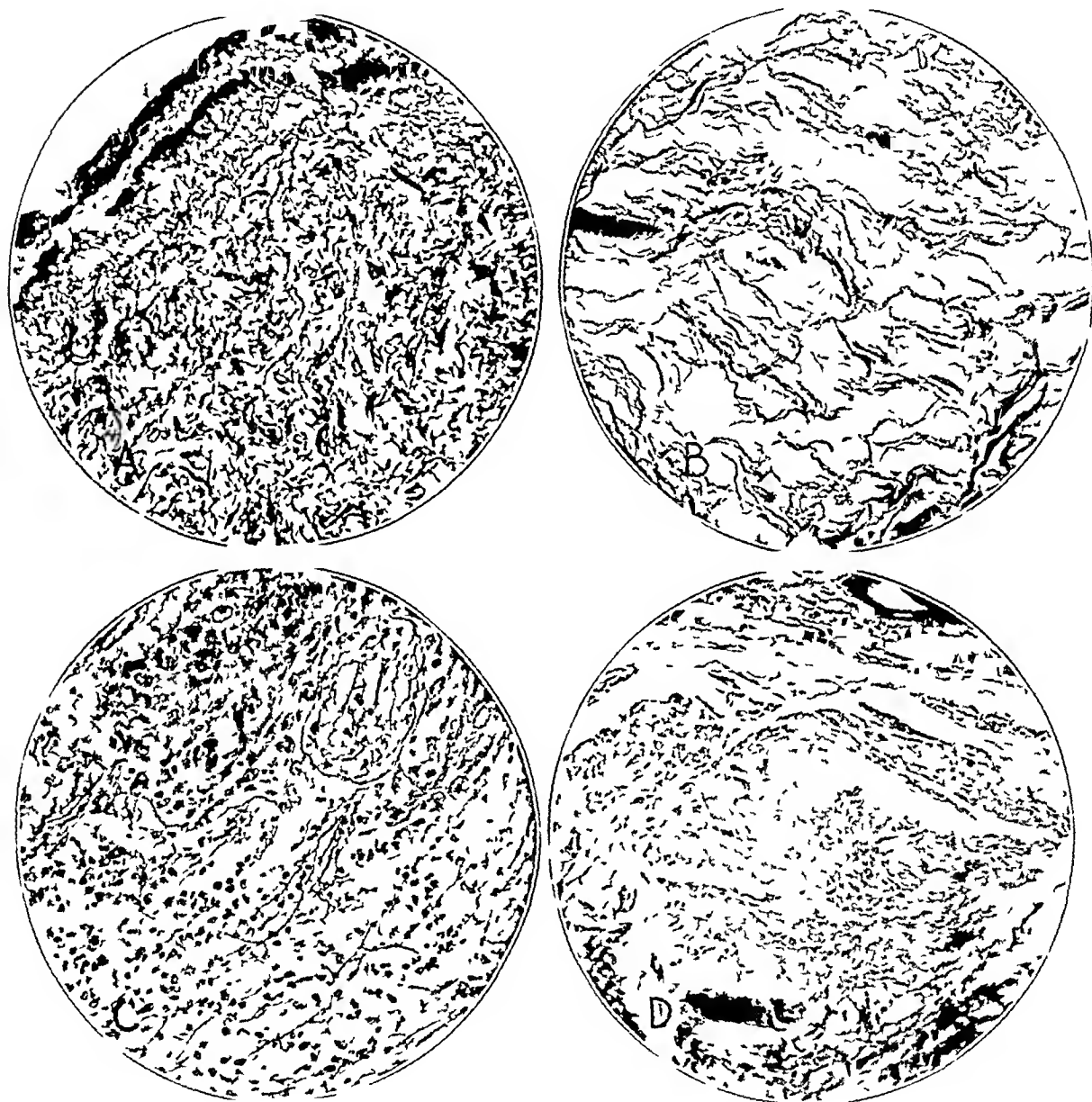


Fig 1—A, fetal tissue (8 months). Section showing fetal type of fibers. Note the absence of the lattice-like arrangement. Stained by Foot's silver impregnation method. B, normal adult tissue. Section showing normal adult precollagenous fibers. Stained by the Maresch-Bielschowsky method. C, squamous cell epithelioma. Section showing typical lattice fibers or pathologic precollagenous fibers. Stained by the Maresch-Bielschowsky method. D, amyloid degeneration. Section showing absence of lattice fibers in the amyloid substance. Stained by the Maresch-Bielschowsky method.

The histologic findings which follow may be regarded as brief protocols. In them, mention will be made only of such variations from the normal or pathologic as are thought to have a bearing, whether direct or indirect, on the reticulum.

#### NORMAL TISSUES

*Skin* In many of my sections, portions of normal skin were included. Lattice fibers were not observed in any of them, in spite of the report of Ferguson<sup>5</sup> that they occurred normally at the dermoepidermal juncture.

*Apocrine Glands*—The fibers around the glands were of the normal precollagenous type such as is seen in slowly growing, noninflammatory tissue.

*Fetal Skin*—The tissue came from 2 fetuses, 5½ and 8 months old. Many immature, young collagen fibrils were present which bore a close resemblance to reticulum fibers but differed from them in the following respects: 1 They failed to stain jet black with silver and were readily impregnated by Van Gieson's stain. 2 They lacked the lattice-like arrangements. 3 The fibrils were longer, had tapering ends and showed a tendency to curl.

*Normal Adult Liver* The classic extensive network was present which gives support to the hepatic cells.

*Normal Adult Lymph Node*—The reticular fibers ramified through all parts of the node and formed networks of varying densities in different areas. These networks were especially dense and narrow meshed on the inner surface of the capsule, on the surface of the trabeculae, around the adventitia of the arteries and veins and throughout the parenchyma. The reticular fibers were more or less scanty within the center of the cortical follicles.

*Normal Adult Spleen*—Around some of the vessels and extending from their walls, networks of reticulum fibers could be seen which were so extensive that they appeared to reach from vessel to vessel. Although splenic tissue is especially adaptable for cell studies with reference to the origin of argyrophil fibers from reticular cells, in no instance could such an origin be clearly demonstrated.

#### CONGENITAL MALFORMATIONS

*Nevus Pigmentosus*—Seven cases were studied. In 2 there was not any reticulum, while 5 contained dense reticulum. In 2 of the 5 there was also collagenous degeneration, which in itself could account for the presence of lattice fibers. The other 3 had a history of recent increase in size. From the standpoint of origin of the fibers, no connection could be demonstrated between the fixed cells and the reticulum. The two

nevi which were devoid of reticular fibers were known to be of slow growth. The rapidly growing ones showing collagenous degeneration had especially dense reticular networks.

*Blue Nevus* In one specimen, the fibers were of the normal, pre-collagenous type and failed to stain with silver. The nevus cells were

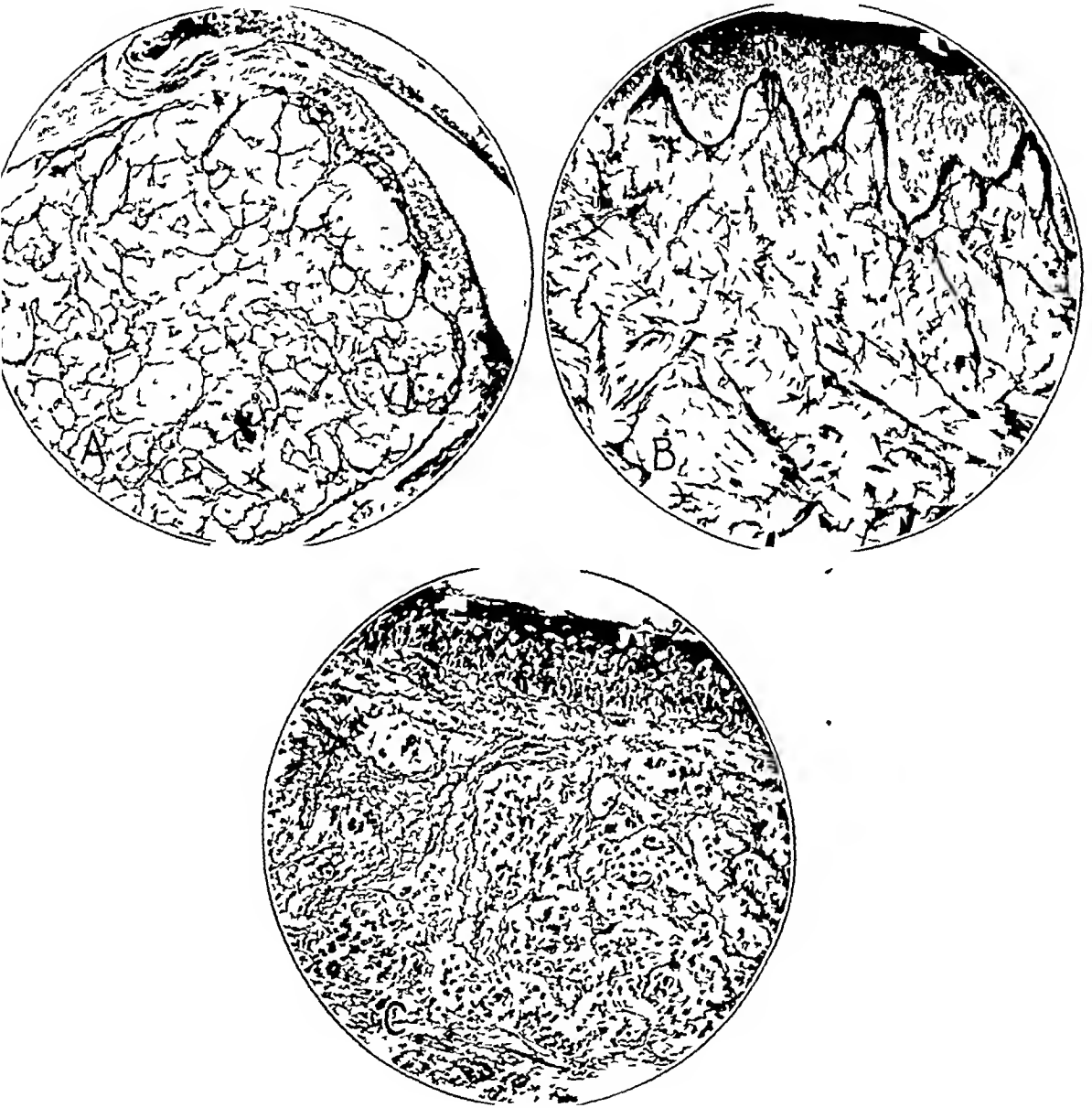


Fig 2—*A*, nevus pigmentosus. Section showing normal precollagenous fibers. Stained by the Maresch-Bielschowsky method. *B*, nevus pigmentosus. Section showing a stroma that borders on the pathologic side. Clinical history of recent increase in size of the nevus. Stained by the Maresch-Bielschowsky method. *C*, nevus pigmentosus with collagenous degeneration. Section showing numerous typical lattice or reticulum fibers. Clinical history of recent increase in size of nevus. Stained by Foot's silver impregnation method.

located in a dense stroma which was free from inflammatory changes. In a second one, which was inflammatory and rapidly growing, numerous lattice fibers appeared in the papillary and subpapillary layers.

*Nevus Verrucosus*—All three of the lesions studied failed to show reticulum fibers and were therefore believed to be of slow growth

#### ATROPHIES

*Radium Atrophy* The tissue came from a 75 year old woman. Twenty years previously she had received a radium treatment for a basal cell epithelioma of the forehead. There was extensive collagenous degeneration of the papillary and subpapillary layers with vascular dilatation. Many of the collagen fibers stained blue with iron-hematoxylin and appeared curled and broken. A sharp line of demarcation existed between the atrophic and normal tissues. Although the cells within the dermis appeared normal in number, a dense reticulum fiber network was present where collagenous degeneration had taken place and was completely absent in the adjoining nonirradiated tissue.

#### DEGENERATIONS AND INFILTRATIONS

*Acanthosis Nigricans*—The specimen came from the axilla of a 50 year old woman. There was no evidence of visceral malignant growth. The upper part of the dermis contained a dense mass of fibers of the lattice type which stained a deep black and displayed the usual netlike arrangement.

*Collagenous Degeneration in a Sebaceous Nevus* (Cheek)—Although inflammatory changes could not be detected, a dense lattice fiber network extended throughout the areas of degeneration and around the sebaceous glands. Their location appeared to be independent of the blood and lymph vessels and also of the nevus and other fixed cells.

*Amyloidosis of the Skin*—The tissue came from the collection of Memmesheimer. Although the masses of amyloid degeneration did not contain reticulum fibers, a few normal precollagenous fibrils were present at their periphery.

*Colloid Milium*—The lesion occurred on the dorsum of the hand of a 45 year old man. Staining by various methods revealed that collagenous degeneration and the reticulum fibers appeared simultaneously and that the location of the first limited the location of the second. Few fixed cells could be detected within these localized or sharply circumscribed colloid masses, and vessels were absent.

*Myxedema*—The tissue came from the ankle of a Chinese man aged 30. The fibrils were of the normal type, although believed to be rapidly growing, they failed to stain jet black with silver and lacked the lattice-like arrangement.

*Xanthoma Tuberosum Multiplex* (Buttocks)—Lattice fibers in moderate numbers occurred about the vessels and within the areas of

lipid infiltration Many other fibers simulated those of the lattice type but failed to stain with silver

*Eczema (Breast)* In this patient, a 46 year old woman, cancer of the breast developed two years later Dense, perivascular networks of reticulum occurred in profusion throughout the entire dermis This reticulum, although present among the infiltrating cells, failed to show a cellular connection or evidence of origin within cells Mitoses were numerous, and in several instances macrophage-like cells could be seen in various stages of penetration of vessel walls

*Scleroderma* The tissue came from the back of a 32 year old woman Lattice fibers were completely absent

#### SPECIFIC INFECTIOUS GRANULOMAS

*Actinomycosis (Neck)* In spite of the dense, granulomatous infiltration which characterizes this disease and the abundance of lattice fibers in certain parts of the lesion, many of the heavily infiltrated areas failed to show the argyrophil fibers, nor did they always occur in abundance about the blood vessels

*Rhinoscleroma (Nose)* Although the infiltrating cells were mostly of the plasma type, numerous Mickulicz cells, macrophages and lymphocytes were present Yet, where the infiltration was densest lattice fibers were greatly decreased in number in contrast to other areas containing thick lattice fiber growths and scanty cellular infiltrations

#### NEW GROWTHS

*Angiosarcoma* The tissue was composed largely of new blood vessels The infiltrating cells were endothelial in type and few in number Elastic fibers were completely absent and the reticulum scanty

*Basal Cell Epithelioma* The general structure was uniform in all the 4 cases The masses of cancer cells were surrounded by dense networks of reticulum, in the meshes of which there were numerous lymphocytes and the macrophage type of cell This network was equally dense irrespective of whether the infiltration was scanty or thick In no instance did this lattice-like structure form a stroma for the invading cells Although basal cell epitheliomas are relatively benign, only one out of the many examined showed normal precollagenous fibers forming at the border of the invading cancer cells

*Granuloma Pyogenicum* The tissue was composed largely of newly formed blood vessels, although one area contained a few infiltrating cells, endothelial in type, together with an occasional lymphocyte, reticulum fibers taking the silver stain were few in number Tumors composed of new blood vessels rarely show a profusion of lattice fibers

*Fibroma (Arm) and Recurrent Fibroma (Wrist)*—The elastic fibers in the recurrent fibroma were decreased or absent, depending on the amount of fibrous tissue in any one area. Where mild inflammatory changes existed, a few lattice fibers could be detected. However, in a separate area, where an intradermal hemorrhage had occurred a few hours prior to the removal of the tissue, a fine, dense reticular network had already formed. The fibroma of the arm contained a stroma which stained a purplish to brownish color with silver and was of the normal precollagenous type.

*Fibrosarcoma (Anus)* Reticulum fibers occurred in abundance within the tumor mass and especially around the blood vessels and sweat and sebaceous glands. The amount of the collagenous stroma in this type of growth appears to influence the density of the developing reticulum fibers.

*Fibrosarcoma (Ear)*—The precollagenous fibers were apparently of the normal type, because they failed to take the silver stain. The absence of lattice fibers in a lesion in which macrophages or phagocytic cells, blood and lymph vessels exist is significant in view of the present accepted theory of origin, as they are generally believed to arise from these cells or from the endothelium of the vessels.

*Glioma Tumor (Forearm)*—The tumor appeared to be noninflammatory. Collagenous degeneration, however, was present, and it was in such areas that reticular fibers occurred in moderate numbers.

*Leiomyoma*—In all 3 cases the fibers were of the normal precollagenous replacement type.

*Lymphosarcoma (Arm)*—Although the sections contained an extensive lattice fiber growth, which was most pronounced in the heavily infiltrated areas, no connection could be seen between the cells and the fibers from the standpoint of origin.

*Melanoma (Ankle)*—There was a thick stroma of reticulum fibers whose density was neither proportional to the number of the tumor cells nor apparently influenced by the presence or absence of blood vessels.

*Melanoma? (Foot)*—Microscopically, this lesion was regarded as an actively growing junction type of nevus. Many of the cells in the nest appeared to be proliferating, while some in other parts of the section seemed quiescent. The areas showing evidence of rapid growth contained reticulum fibers not only among the pigmented cells but also at their periphery. The best example of this apparent attempt to limit growth is seen in basal cell epitheliomas.

*Squamous Cell Epithelioma*—Reticulum fibers were especially dense, irrespective of the type or number of infiltrating cells and their location.

Although in some instances the fibers appeared to wall off the cancer cells, this did not occur in the highly malignant tumors whose stroma was largely made up of the same kind of lattice fibers. In one lesion the reticulum fibers appeared to be continuous with the walls of the lymph and blood vessels, yet unattached to the infiltrating cells including the macrophages.

#### RÉSUMÉ OF STUDIES OF TISSUE

1 In no instance in the hundreds of sections examined could it be clearly demonstrated that reticulum fibers arose from or were directly connected with either the infiltrating or the fixed cells of the dermis.

2 Although reticulum fibers frequently appeared to be continuous with the walls of the blood vessels, they were able to develop in areas distant from blood vessels and devoid of infiltrating cells.

3 The presence of reticulum in certain organs that are normal is not incompatible with the theory that some factor such as an enzyme leads to their development and that such a factor is elaborated by the cellular constituents.

4 As to primary degenerative disease in the skin, areas of amyloid degeneration did not contain reticulum fibers, and they were also absent in myxedema.

5 On the other hand, all areas of collagenous degeneration studied contained reticulum fibers, and the two appeared to develop simultaneously. This development was best illustrated in colloid milium, in which a slight decrease in the density of the fibers was also noted in the older nodules.

6 The number of reticulum fibers in pathologic tissue did not parallel the density of the infiltrating cells, their scantiness in certain parts of the sections of actinomycosis and rhinoscleroma suggests that under certain conditions toxins are present which are capable of inhibiting their development.

7 An important factor in determining the number of reticulum fibers in pathologic conditions of the skin, especially tumors is the amount of collagenous stroma present.

8 Growths composed largely of new blood vessels such as the angiosarcomas and pyogenic granulomas contained few reticulum fibers.

9 Reticulum fibers in pigmented and similar nevi are an indication of rapid growth.

10 Argyrophil fibers were absent in dermatoses (for example, keratosis palmaris et plantaris) whose pathologic changes were limited to the epidermis and in such diseases as pityriasis rosea, in which only slight dermal variations from the normal occur.

## COMMENT

The findings just recorded for the skin may be arranged into two groups first, those which bear on the histogenesis of reticulum fibers and, second, those which have significance in disease

*Histogenesis* The phenomena support the theory of Plenck<sup>15</sup> that the reticulum fibers in normal tissue, such as liver, spleen and lymph nodes, represent a third kind of connective tissue and that they have mechanical qualities different from collagenous and elastic elements, so that they originate (and after that persist) when the functional demands on the tissue make it desirable

Too, according to Maximow and Bloom,<sup>16</sup> many histologists have pointed out that "when the first intercellular fibrils develop in the embryo, they often make their appearance without any apparent relation to the cells. They are first seen far from the cell bodies, in the structureless, liquid or jelly-like substance which fills the free spaces in the mesenchyme and which is undoubtedly a passive, lifeless material secreted by the cells. Nor is contradictory the fact that it is possible to obtain collagenous fibers in connective tissue cultures growing outside the body. Apparently the development of collagen in an embryo, in young scar tissue and in tissue culture, is identical in principle." The appearance of a dense reticulum around blood vessels within such a short time as forty-eight hours (Way and Klovekorn<sup>7</sup>) further strengthens the theory, the development of formed structures at a rapid rate is more consistent with processes that are of the order of "precipitation" than with the slower processes which involve biologic activity of cells. I should take a step further by offering the hypothesis that the "gelation" is mediated by a factor or hormone which acts on an enzyme produced by the reticular cells of liver, spleen, lymph nodes and other organs and that the phenomenon is possibly analogous to the mechanism in fibrin formation. Such a hormone would exist in a more concentrated form at its site of origin and in more dilute form in the blood stream. The appearance of reticulum fibers first around a blood vessel may imply that it is here that the activating factor first comes in contact with the amorphous ground substance.

The evidence favoring this enzymic theory is as follows. First, the reticulum fibers can occur in regions where there are not cells of any kind, including those of the reticuloendothelial system, such as the regions of collagenous degeneration which were frequently not associated with inflammatory changes. It would be especially difficult to explain an origin of the fibers from reticuloendothelial cells and vascular endo-

15 Plenck, H. Ueber argyrophil Fasern (Gitterfasern) und ihre Bildungszellen, Ztschr f d ges Anat (Abt 3) 27 302, 1927

16 Maximow and Bloom<sup>8</sup> p 100

thelium in such regions, moreover, my findings show that they need not even be in the immediate vicinity of blood vessels. Second, tissues containing heavy inflammatory infiltrations, including macrophages, do not necessarily contain dense reticulum, this might speak for the necessity of a factor of specificity on the part of the cells in the direction of enzyme production. This theory is submitted only as a theory and with the full realization that physiologicocochemical tests are necessary to test what it may be worth. It may, though, serve as a point of departure.

*Dermatopathology* Reticulum fibers were absent in myxedema, in amyloid degeneration, in conditions limited to the epidermis and in such diseases as angiokeratoma, keloid, keratosis follicularis, molluscum contagiosum, neurofibroma and syringoma. According to my theory such absence could be due to lack of enzyme in these lesions. This deficiency might be explained on the basis of lack of need for rapid replacement of tissue or because of the presence of inhibitory toxins. As to nevi, it will be recalled that reticulum appeared in rapidly growing ones. Inasmuch as this was the case whether inflammatory changes were present or not, its presence has prognostic value, particularly in the cases in which the inflammatory changes are lacking.

#### CONCLUSION

There are reasons for the hypothesis that reticulum fibers originate in a lifeless colloidal sol in the tissue spaces as the result of a hormone-enzyme interaction. On the basis of my materials, normal fetal and adult dermal tissues are devoid of reticulum fibers.

The ability of precollagenous tissue to take the silver stain is dependent on its age and rate of growth.

Conditions as to reticulum may be significant in several dermatoses. 1 When present in nevi (which may be the case even in the absence of inflammatory reactions), it indicates rapid growth. 2 The fact that, in dermatoses of exogenous origin they develop first in the papillary layer of the dermis may be significant in evaluation of those due to primary irritants and those of hematogenous origin. 3 The presence of reticulum fibers within areas of collagenous degeneration and their absence in myxedema serve to differentiate one from the other.

#### ABSTRACT OF DISCUSSION

DR FRED D WEIDMAN, Philadelphia. The large material presented by Dr Way is eloquent of the strong foundation for the findings which he has reported, and the lantern slides also speak for some of the diagnostic results which have come from his studies, particularly in the matter of the diagnosis of rapid growth in nevi (and the potentialities therein) even before inflammatory infiltration has developed in connection with it.

It must be remembered that there is a difference between reticulum, on the one hand, and reticuloendothelial tissue, on the other. Reticuloendothelial tissue is

obvious in hematoxylin and eosin sections, but the reticulum fibers, such as Dr Way has been discussing, are not visible, a silver technic is necessary

It is regrettable that reticulum stains are not employed more commonly in dermatologic circles. The technic is not too difficult, and yet technicians commonly shv from it. A simple and satisfactory one is included in "Approved Laboratory Technique" (Kolmer, J. A., and Boerner, F., ed 4, New York, D. Appleton-Century Company, Inc., 1945). Variant 1, described on page 942, is the one I use.

Finally, there is an increasing interest in the diseases of connective tissues. For years, the epithelial ones have dominated the medical scene. Recently, the Russians have been active in the development of antireticulocytotoxic serum in the treatment of various diseases, and I know of one dermatologist who is now investigating its usefulness in the cutaneous field. It is indeed welcome to have more and more data submitted as to the possible functions of these much neglected tissues, and Dr Way has rendered a service in submitting this thesis of an enzymic property which leads to the production of reticulum.

DR HAMILTON MONTGOMERY, Rochester, Minn. Dr Way has pioneered in the study on reticulum, or lattice, fibers. He once wrote a paper on grading of cancer of the skin by reticulum stains. In an unpublished study of a series of cases of basal and squamous cell epithelioma, I was able to confirm Dr Way's findings and found that classification by use of Maresch-Bielschowsky staining checked with Broder's classification of gradation and that the two methods of classification intergraded perfectly. As Dr Weidman has stated, however, one must have a good technician to obtain a good Maresch-Bielschowsky stain or any modification thereof.

I make use of this stain frequently. I found that lupus erythematosus shows involvement of the reticuloendothelial system but also a definite increase in reticulum fibers. There is also increase in reticulum fibers in mycosis fungoides and Kaposi's sarcoma, and perhaps one might find it in eosinophilic granuloma, although I did not have the opportunity to make reticulum stains in a case I had the opportunity to study. In regard to the epithelial versus the neural origin of nevi, it must be remembered that the Maresch-Bielschowsky method stains reticulum and nerve fibers indiscriminately. There is another silver stain, Bodian stain, which will stain nerve fibers and not reticulum fibers.

DR STUART C. WAY, San Francisco. First of all, I should like to thank the discussers, especially Dr Weidman, who made many valuable suggestions during the preparation of this paper.

Dublin, in a recent paper entitled "Reticulum" (*Arch Path* 41:299-318, 1946), stated that reticulum is probably formed by intercellular precipitation of a secretion produced by reticular cells, histiocytes, monocytes, lymphocytes, vascular endothelium, fibroblasts and both smooth and striated muscle but did not explain the mechanism of the process. In other words, his studies tend to confirm my impression that the development of formed structures at a rapid rate is more consistent with processes that are of the order of "precipitation" than with the slower processes, which involve biologic activity of cells.

I might also add that there is a difference in reticulum formation in syphilis, referring to the chancre and the gumma, and that in tuberculosis of the skin, the growth being much denser in syphilis.

# ROLE OF FOOD ALLERGY IN ECZEMATOID DERMATITIS

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**T**HE TERM "eczematoid dermatitis" is used in this paper to denote a group of somewhat heterogeneous dermatoses of various morphologic types which are eczematous in character and resistant to treatment and do not belong to any other, more clearly delineated, clinical picture. It is well recognized that multiple etiologic factors often contribute to the production of eczematoid dermatitis (Stokes<sup>1</sup>). The present paper deals with one of these factors, namely, food allergy, which we have demonstrated to be the primary factor in a number of cases. Thirteen cases in which the offending foods were discovered by trial or elimination diets are reported. Ingestion of these foods caused an exacerbation of the dermatitis within twenty-four hours. Elimination of these foods was followed by prompt healing of the cutaneous lesions.

Approximately half the patients referred because of cutaneous diseases to a general hospital in the southeastern United States suffered from eczematoid dermatitis of the hands and feet. These patients were admitted with a variety of diagnoses: "nummular eczema," "contact dermatitis with secondary infection," "dyshidrotic eruption of the hands and feet," "pompholyx," "dermatophytosis of the hands and feet with secondary infection," "contact allergy" and "recurrent vesicular eruption of the hands." They had had numerous and prolonged periods of hospitalization. A few responded to local treatment, control of emotional problems, elimination of contact allergens, clearing up of pyogenic secondary infection or removal of foci of infection. However, in many cases these measures failed to produce any lasting improvement. The patients continued to have active patches of dermatitis, which gradually became larger, and new patches continued to appear. Routine scratch and intradermal tests were of little value. The lack of lasting improvement after all other etiologic factors had been removed or reduced to a minimum made us believe that food allergy was playing a definite role in the

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1 Stokes, J H, Lee, W E, and Johnson, H M. Contact, Contact-Ineffective and Infective-Allergic Dermatitis of the Hands, *J A M A* 123 195 (Sept 25) 1943.

production of the dermatitis. With an excellent opportunity to observe the patients closely while they were on trial diets, several patients with severe eruptions were tested, and the results were most gratifying. It was found that the dermatitis flared up dramatically when certain specific foods were ingested. Consequently, we have continued our studies along these lines.

#### METHODS

Three different methods of determining the reactions to food substances were used: (1) the strict trial diet, (2) the elimination diet and (3) the food diary.

1 *The Strict Trial Diet*—The strict trial diet is carried out by strict elimination of all food for twenty-four hours and daily testing with simple foods. It is by far the best method, but it is the most difficult for the patient and usually requires hospitalization. It is applicable to all types of eczematoid dermatitis and may be used in any stage of the process provided secondary infection, when present, is under control with local treatment and sulfonamide compounds taken by mouth or penicillin received intramuscularly. The method used is essentially the same as that outlined by Stokes<sup>2</sup> except that milk or buttermilk is not used as the initial food. The purpose of the experiment, the method of application of the diet and the methods of evaluating results are explained to the patient, and the responsibility of adhering to the diet is transferred to him. The following plan is then followed:

1 He is given castor oil (45 cc.) if there has been a recent flare-up and is allowed to have nothing by mouth for twenty-four hours except water, to which a little sugar may be added.

2 After the first twenty-four hours there is usually an improvement in the patches of dermatitis, less itching and few or no new vesicles. The patient is then allowed to have his first food, usually potatoes. Salt may be used but no pepper or butter. He receives only potatoes on this day.

3 On the third day the patches of dermatitis are inspected for flare-ups, which will be evidenced by (a) increase in itching coming on two to eight hours after the intake of food, (b) erythema of the patch, (c) new vesicle formation and (d) weeping of the patch. It is important to be able to distinguish new vesicles from the old ones, and after a little practice this is easily done. The new vesicles are in various stages of development, especially in regard to size, their walls are usually taut and translucent and the fluid clear. New vesicles have a zone of erythema which fades in twelve to thirty-six hours, then the top becomes brown or yellow, and the tenseness of the vesicle is lost. The new vesicles usually appear on the site of the dermatitis, but new patches may develop at any time, especially with a severe reaction. Weeping of the patch usually occurs only with severe reactions, and when it does occur it means that it will take three to four days for the flare-up to subside. If none of these signs are discovered the patient is allowed to continue with potatoes, and a new food is added. The second food selected is usually beef.

4 The patches of dermatitis are inspected daily, and as long as there is no flare-up a new food is added each day. When a reaction does occur the time of its onset and its severity are noted, and use of this food is discontinued. The food may be tested again at a later date.

2 Stokes, J. H. *Fundamentals of Medical Dermatology*, ed. 7, Philadelphia, Department of Dermatology Book Fund, 1942, p. 218.

5 When there is a questionable reaction, the food is either continued for one or more days without the addition of a new food or discontinued and tested at a later date

6 With some foods the reaction will be severe and will require two to four days for the flare-up to subside. During this period no new foods should be added. It is unfortunate if such reactions occur early in the testing, but such adversity is usually overcome and the patient is willing to continue with the few foods that are allowed until the flare-up subsides and he is again ready for testing.

7 After the diet has progressed for several weeks a persistent but mild flare-up may appear daily. This usually means that a food is being taken to which the patient is mildly sensitive and which was overlooked during the testing. In such cases the diet is reviewed, and a list of foods is made for a basic diet. This list should contain only foods which the medical officer and the patient feel have been nonoffenders on previous testing. The basic diet is continued for four to six days, and after sufficient improvement new foods are added or questionable foods are retested.

8 In the beginning only simple foods—potatoes, beef, pork, the various fruits and vegetables, milk, eggs and wheat—are added, and after the diet has progressed sufficiently mixtures of foods, such as salads, bread and cake, may be used.

9 When pork is added, the patient may have bacon, ham and, later, sausage. Wheat is best tested by the use of Cream of Wheat. Dry cereals should be tested late in the diet because of the variety of flavoring materials added to such cereals.

10 The responsibility of keeping the diet is placed entirely on the patient. In most cases this cooperation is excellent, even from persons with lower than average intelligence. One or two definite flare-ups following a period of quiescence serve to convince even the most skeptical persons that they are on the right road and that recovery will follow strict adherence to the diet. Most of the patients, having suffered from the dermatitis for a long period with little relief in the past, are grateful for improvement. Occasionally a patient will cheat, but this can usually be suspected. The patient is not accused of cheating, but with every flare-up the last food added is removed, and soon the patient realizes that his diet is being restricted so much that cheating is not worth while. This is more effective in overseas theaters, where post exchange supplies are rationed and extra food is not available.

11 A good dietitian is of great value in helping the patient select foods, in preparing a small group of foods in a variety of appetizing ways and in seeing that the patient gets enough to eat.

12 After the first few weeks the patient learns to recognize exacerbations, and he can continue testing foods on his own initiative. He is taught the various ingredients of complex mixtures and is made to realize that if he is sensitive to eggs he cannot eat cake, custards, ice cream and other foods containing eggs. The strict trial diet is by far the most exact method of determining food allergy. It is the most difficult to carry out and usually requires hospitalization. Full cooperation of the patient is necessary, and frequent assurance by the medical officer helps the patient over the most difficult periods. This method is applicable to all types of persons in good nutritional state. Early in the treatment there is some loss of weight but this is usually not serious, and supplementary vitamins are not necessary. If they are used they must be tested like other substances. This is particularly true of vitamin B complex.

The following 2 cases illustrate the use of the strict trial diet

CASE 1 (12 in table) —A nurse aged 24 suffered from a pruritic papular and vesicular eruption of her fingers for approximately one year. She had received local treatment, with little improvement. A series of cutaneous tests were made shortly after the onset, and she had positive reactions to a group of sea foods and cheeses. Elimination of these foods produced no improvement. When she was first seen in our section, she had numerous excoriated papules and vesicles on the dorsum and sides of her fingers, extending down and involving the webs. She also had a few excoriated papules in the axillary folds and some about the abdomen. She was given a course of antiscabies treatments with a preparation of sulfur, but this failed to produce any improvement. She was then given a strict trial diet, and after a twenty-four hour period of starvation there was decided improvement and almost complete absence of pruritus. She was then allowed to have potatoes, which produced no flare-up. The next day she was given beef, with no reaction. On the fourth day she requested coffee rather than a vegetable and took three cups of coffee during the day in addition to potatoes and beef. During the night she was awakened by an itching of the hands, and the next morning she presented patchy erythema, vesiculation and excoriation of the fingers. Coffee was removed from her diet, and other foods were added successively each day, without a flare-up. After two weeks of being tested and being found sensitive only to coffee she was given a full diet with the exception of coffee, and her hands remained clear. Coffee was tried again after one and after two months and provoked a reaction each time. No attempt was made to determine whether the allergen was coffee or an added flavoring agent such as chicoriv.

This case illustrates a patient's sensitivity to one common food, its detection by the trial diet and cure of the dermatitis by elimination of the offending food.

CASE 2 (5 in table, fig 1) —A 27 year old white soldier began to have a pruritic dermatitis in the third interdigital space of his left hand in June 1944. During the next six months the eruption progressively spread to the lateral border and the third and fourth fingers of his left hand. Multiple types of local therapy were utilized, without affording relief. He was admitted on two separate occasions to a forward field hospital, each admission lasting for three weeks. Local and general therapy at that installation had no effect, so he was transferred to our section in a general hospital. An examination on his admission disclosed acute, denuded, oozing, crusting, patchy eczematoid dermatitis of all surfaces of the third and fourth fingers, all the interdigital spaces and the entire palmar surface of the left hand, the volar surface of the left wrist and the right thenar eminence. The next thirty days were utilized in treating the pyogenic element, and at the end of this period there remained erythematous, dry, scaling patches, moderately to mildly pruritic, with transitory discrete vesicles. He was given a strict trial diet and for twenty-four hours had nothing by mouth except water. On the following day potatoes were added, with no reaction resulting. Next, beef was added to his diet, again without subjective or objective changes. At daily intervals thereafter, tea, bread, chicken, string beans, Cream of Wheat, milk and chocolate were added, without change, except that the pruritus entirely disappeared and vesicles were no longer present. The next food added was a mixture of grapefruit and orange juice, which he drank at the noon and evening meals of the day. About nine hours after the

latter meal his hands began to burn. This burning continued unabated throughout the night, and on the following morning there was a definite increase in the erythema and small denuded areas appeared at the sites of the original cutaneous involvement, particularly on the dorsal surfaces of the fingers of the left hand and the right thenar eminence. Use of all fruit juices was discontinued, and the reaction subsided in thirty-six hours. The denuded areas epithelized in four days. Next, coffee and rice were added and produced no reaction. Eggs were then added to the diet and eaten at the evening meal of the same day. On the following morning the patient had many new vesicles, estimated at fifty, and an increase in the erythema of the palmar and dorsal surfaces of the third and fourth fingers of his left hand. Eggs were discontinued. The vesicles were dry in thirty-six hours and disappeared in seventy-two hours. Pork was next added and eaten at the noon meal. Ten hours later his hands were moderately pruritic, and the following morning he had many new vesicles of the palmar surface and the third and fourth fingers of his left hand. Pork was eliminated, and the vesicles disappeared in seventy-two hours. Butter, cabbage, macaroni, tuna fish, peas, carrots, wheat cereal (dry) and salmon were successively added at daily intervals without producing a reaction. Peanuts, tomatoes, tomato juice and cheese produced exacerbations similar to those following eggs. Grapefruit and orange juice also produced flare-ups when retested separately. At the completion of this study there was only residual lichenification at the original sites of involvement. After complete testing and retesting, the patient was found sensitive to orange juice, grapefruit, eggs, pork, peanuts, tomatoes and cheese. As long as he avoided these foods, his dermatitis remained in abeyance.

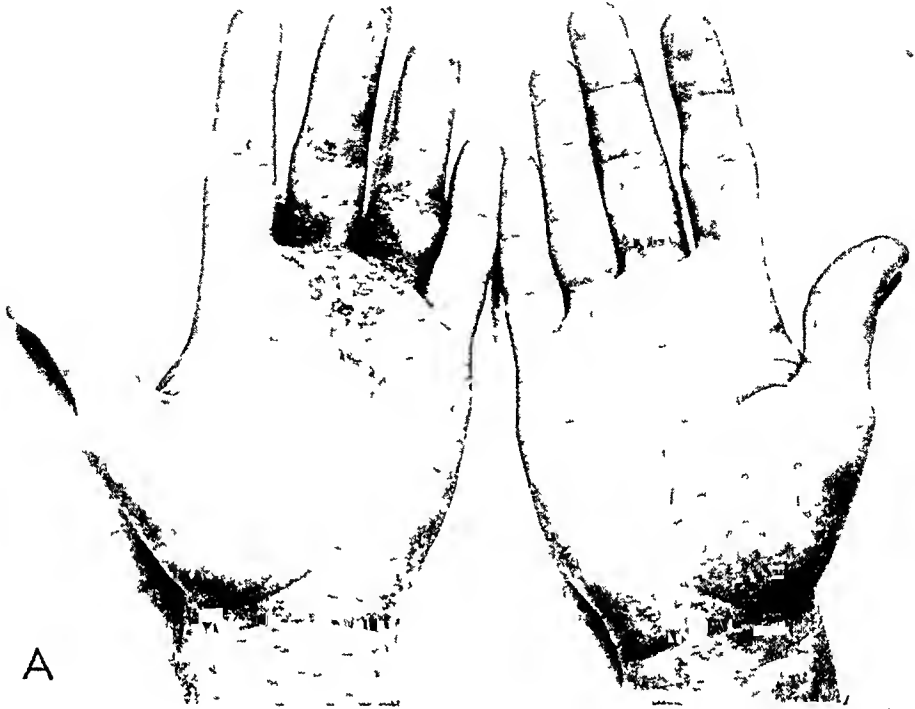
This case illustrates the role of multiple food allergens in producing eczematoid dermatitis of the hands.

*2 The Elimination Diet*—The second method is similar to that proposed by Rowe,<sup>3</sup> in which the patient is given a basic diet consisting of supposedly non-allergenic foods. It is applicable only in cases in which there are few sensitivities. Our experience with the trial diet indicates that it is extremely difficult to select a basic trial diet which will not contain at least one food to which a patient is sensitive. After the patient has been on the basic diet for one week, there should be a definite improvement in the dermatitis. If this is not evident, the procedure might as well be abandoned. When improvement is manifest, foods are added and observations are made daily, as in the case of the trial diet. Thus the only essential difference is that in the trial diet we start with no food at all whereas in the elimination diet the patient is allowed a basic diet made up of a combination of foods which one hopes will not contain allergens. The choice of the basic diet will depend on the food available and the patient's past experience with known sensitivities to food.

The following report of a case illustrates the use of this method.

*CASE 3*—A 30 year old white soldier had a pruritic, patchy vesicular dermatitis of his right hand approximately one year before his admission to the hospital. The lesions showed exacerbations and remissions and spread to the fingers of his left hand. Multiple local therapeutic agents were utilized, and he spent one month in a forward field hospital, where all therapy proved to be valueless.

*3* Rowe, A. H. *Food Allergy Its Manifestations, Diagnosis and Treatment*, Philadelphia, Lea & Febiger, 1931.

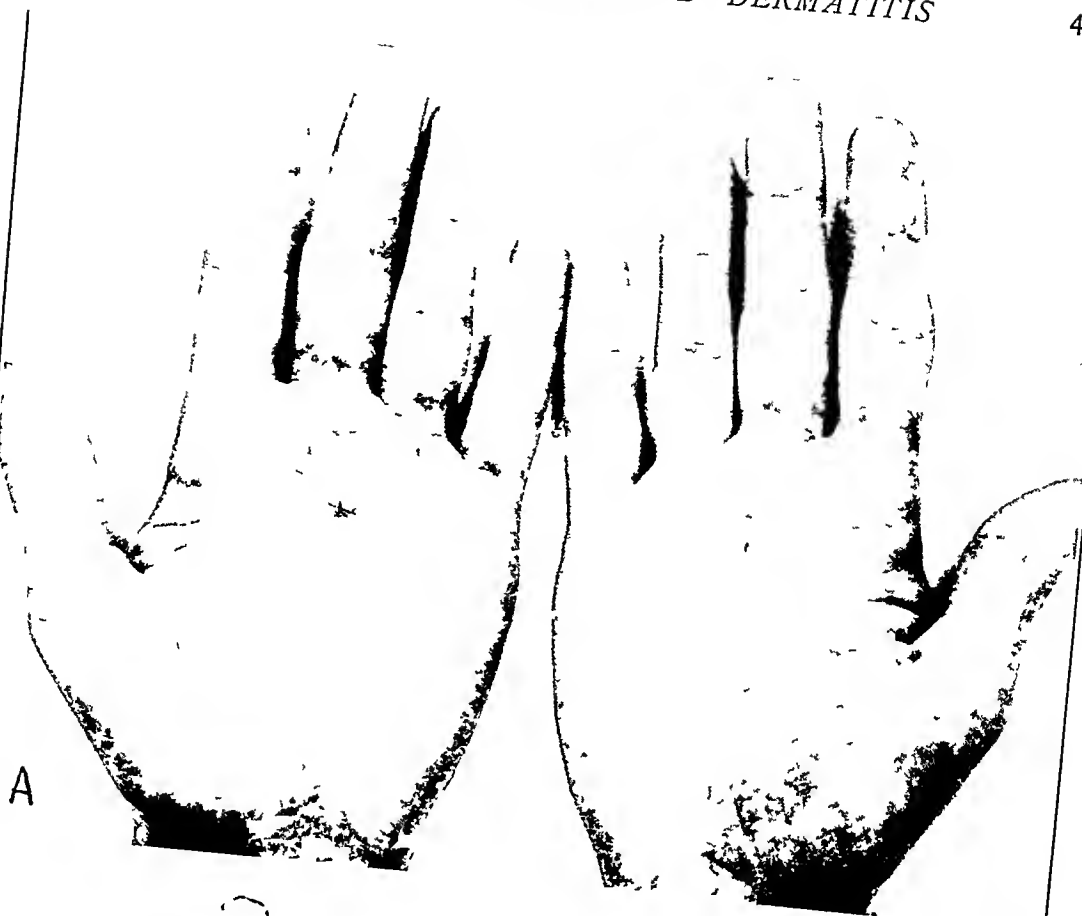


A



B

Fig 1 (case 5)—Acute eczematoid dermatitis of the palms and dorsa of the hands as it appeared on March 20, 1945



A



B

Fig 2 (case 5) —An improvement in the dermatitis as seen on May 18, 1945, following a trial diet and elimination of string beans, eggs, oranges, pineapple, tuna fish, tomatoes, beets, American process cheese, pork, grapefruit, asparagus and baked beans

On his admission to our section a physical examination revealed no abnormalities except for the presence of patchy eczematoid plaques of dermatitis on the dorsal surfaces and sides of the second and third fingers of his right hand, the second, third and fourth fingers of his left hand, and both thenar eminences. Two days after admission he was given a basic elimination diet consisting of chicken, beef, rice, string beans, potatoes, tea, oatmeal and sugar. This diet was continued for five days, during which time all pruritus disappeared and the lesions regressed about 60 per cent. On the sixth day of the diet mutton was added, without effect on the patient's dermatitis. On the seventh day pork was added. He ate a large slice of pork sausage at the noon meal, and eight hours later he noticed that his hands were burning and pruritic. This eruption gradually became worse and lasted throughout the night, awakening the patient on three separate occasions. On the following morning he had ten new vesicles on his fingers. The original plaques of dermatitis were denuded and more erythematous. Use of pork was discontinued immediately, and in forty-eight hours the vesicles and erythema disappeared and the denuded areas were epithelized. Next, coffee was added to the diet, with no subjective or objective changes. Bread was added on the following day and was eaten at two meals. Six hours after the last meal the original sites of dermatitis began to burn. The next day these lesions showed a decided increase in erythema, and many small denuded areas were seen. Use of bread was discontinued, and the acute reaction subsided in thirty-six hours. Carrots, macaroni, spaghetti, tomatoes, onions, and peaches were added at daily intervals, in that order, without effect on the dermatitis. Next cheese was added and eaten at the noon meal. Eight hours later the patient's hands began to burn, and they continued to do so throughout the night. On the following morning he had fifteen to twenty new vesicles on his fingers and both thenar eminences. Use of cheese was discontinued, and the vesicles dried in twenty-four hours and disappeared in forty-eight hours. A similar reaction was provoked by chocolate, eggs, butter and lemonade. All other foods, including nuts, fish, fruit juices, peas, cabbage and carrots, added at daily intervals, had no subjective or objective effect on the dermatitis. At the end of this study the patient's dermatitis was 99 per cent healed, and all that remained were two small dry, scaling patches, one on each thenar eminence. He has remained free of all dermatitis for one month following the complete elimination from his diet of pork, bread, butter, eggs, cheese, chocolate and lemonade.

3 *The Food Diary*—The third method of determining food allergies is by the use of a food diary. It is applicable only in cases in which there is a more or less chronic eczematoid dermatitis with mild acute exacerbations once or twice a week. The patient keeps an accurate account of every food eaten during the day, both at meals and between meals. After the daily list of foods he records the condition of the skin—"improved," "no change," "worse," "itching," "new vesicles," "weeping" or "new patches." The time of each flare-up is recorded. After the record is kept for two or three weeks, the days of the flare-ups are noted and special attention is given to foods that appear on the list the day before and early in the same day. Certain foods which stand out as possible factors are eliminated from the diet, and after sufficient improvement they are tested by adding one of the foods at intervals of three days.

The following case illustrates this method.

CASE 4 (13 in table)—The patient was admitted to the hospital with several slowly healing leech bites on the lower extremities. After considerable local treatment and excision of one of the fragile scars on the left leg in the middle

part of the shin, the patient suddenly noted a patch of eczematoid dermatitis on the lateral aspect of the left ankle. This was followed in about one week by an eczematous eruption in the groin and the perineum. A variety of local treatments for two weeks produced only slight improvement. It was noted that the dermatitis was of a subacute variety with a low degree of activity but would become acute once or twice a week. The patient was told to keep a diary of the food eaten at breakfast, dinner and supper, which is as follows

April 6	B	Coffee	Skin unchanged
	D	Beef, cabbage, string beans, applesauce	
	S	Beef, potatoes, corn, peaches, coffee	

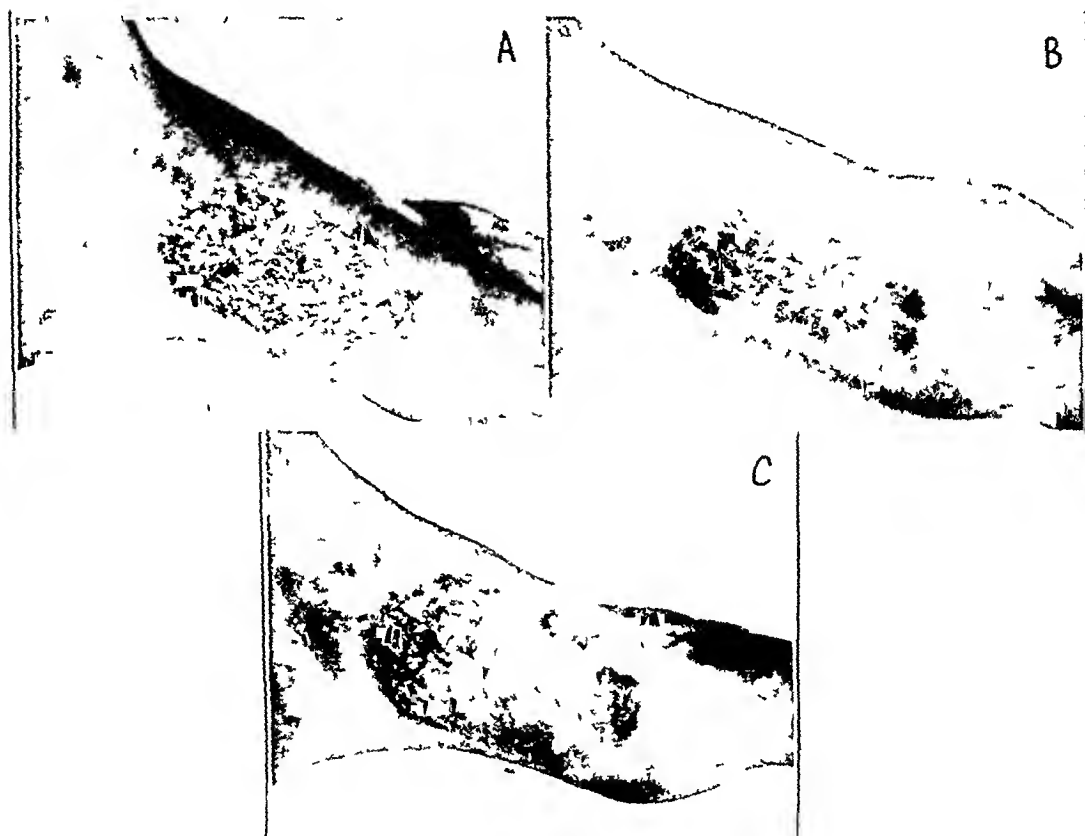


Fig 3 (case 10) — *A*, the appearance of eczematoid dermatitis of the medial aspect of the foot on May 22, 1945. *B*, an immediate improvement three days after the start of the trial diet. *C*, an acute flare-up of the dermatitis twenty-four hours after string beans were eaten on June 2, 1945. Note the crusted appearance at the posterior portion of the lesion and the new vesicles on the anterior section.

April 7	B	Coffee	Skin unchanged
	D	Beef, tea, vanilla pudding, peas	
	S	Chicken, potatoes, coffee, beets, jello	
April 8	B	Prunes, oatmeal, beef, coffee	Skin unchanged
	D	No food	
	S	Beef, potatoes, carrots, figs, lettuce	

April 9	B	Corn flakes, chicken, coffee, applesauce	Area enlarged, more itching, no weeping 4 p m
	D	Beef, potatoes, beets, pineapple, coffee, cabbage	
	S	Chicken, peas, rice, fruit salad	
April 10	B	Bacon, fried potatoes, coffee, grapefruit	Flare-up still apparent
	D	Corned beef, Spam, potatoes, coffee, peaches, cabbage	
	S	Beef, potatoes, asparagus, fruit salad, coffee	
April 11	B	Corn flakes, bacon, prunes, grapefruit, coffee	New patch, flare in old ones—3 p m
	D	Pork sausage, beans, beets, peas, tea, peaches	
	S	Chicken, peas, potatoes, applesauce, milk	
April 12	B	Rice Krispies, prunes, coffee, potatoes	Itching—12 noon Weeping—3 p m
	D	Chicken, potatoes, carrots, coffee, pears, peaches, lettuce	
	S	Beef, asparagus, potatoes, butterscotch pudding, coffee	
April 13	B	Oatmeal, corned beef hash, coffee, applesauce	Flare subsiding
	D	Roast beef, potato soup, rice, pears, milk, butterscotch pudding	
	S	Chicken, potatoes, string beans, fruit jello, coffee	
April 14	B	Corn flakes, pears, potatoes, coffee	Weeping of all patches—2 30 p m
	D	Tuna fish, applesauce, lettuce, potatoes, carrots	
	S	Beef, potatoes, fruit cocktail, corn, coffee	
April 15	B	Rice Krispies, coffee, grapefruit	Weeping worse, patches longer
	D	Pork sausage, peas, pears, potato salad, tea	
	S	Chicken, beets, fruit salad	
April 16	B	Rice Krispies, coffee, prunes	Weeping greater
	D	Potatoes, beef, peaches, coffee, asparagus	
	S	Beef, potatoes, peaches, corn, coffee	
April 17	B	Rice Krispies, coffee, prunes	No change, still weeping
	D	Vienna sausage, kidney beans, carrots, milk, peaches	
	S	Chicken, potatoes, peas, coffee, pineapple	

The diary had been carried on for ten days, with four definite exacerbations, starting on the afternoon of April 9. There was some improvement on April 10 with a flare-up on April 11 and a continuation on April 12. On April 13 there was some improvement, but on April 14, 15 and 16 the patient suffered a prolonged flare-up, with vesiculation, increase in the size of the lesions and weeping. From a review of the record different foods stood out as possible factors. On April 9 and 10 the foods were corn flakes, rice, grapefruit, pork (bacon and Spam). On April 11 and 12 corn flakes appeared for the second time, as also did pork and rice (Rice Krispies). On April 14, 15 and 16 the following foods were suspected: corn, corn flakes, tuna fish, Rice Krispies, grapefruit and pork. Thus the following foods were eliminated from the diet: grapefruit, corn, rice, pork and tuna fish. The diary was continued.

April 18	B	Coffee	Improved
	D	Beef, cabbage, string beans, applesauce	
	S	Chicken, potatoes, coffee, beets, jello	

April 19	B	Creamed beef, applesauce, coffee	Improved
	D	Beef, pears, potatoes, lettuce, beets	
	S	Beef, vanilla pudding, potatoes, peas	
April 20	B	Corned beef hash, applesauce, coffee	Improved
	D	Salmon, potatoes, string beans, milk, peaches	
	S	Chicken, carrots, potatoes, milk, applesauce	
April 21	B	Prunes, coffee	Much improved
	D	Beef, pears, potatoes, applesauce, milk	
	S	Beef, beets, potatoes, fruit jello, coffee	
April 22	B	Beef, peaches, coffee	Improved
	D	Beef, potatoes, string beans, fruit salad, tea	
	S	Chicken, potatoes, lima beans, coffee, peaches	
April 23	B	Beef, pears, coffee	Improved
	D	Chicken, pears, potatoes, fruit salad, lettuce	
	S	Beef, carrots, potatoes, pears, lettuce	

After this improvement it was decided to test the patient with the suspected foods previously eliminated. After eating bacon and pork sausage for several days, he suffered no flare-up. At intervals of three to four days other foods were tested, and he had a reaction to rice, corn and grapefruit juice but none to tuna fish. By his remaining on a diet eliminating corn, rice, grapefruit and chocolate (the patient knew that he was sensitive to chocolate by previous experience), his skin gradually improved and has remained well.

This case is an example of the determination of food allergens by the food diary. Such a method is easy to carry out and works especially well in cases in which the patients have noted definite flare-ups once or twice a week. Such a plan can be carried out on an outpatient basis with the soldier on full duty.

#### COMMENT

We have studied a total of 50 patients with eczematoid dermatitis in which food sensitivity was of primary etiologic importance. The 13 reported on in this paper are those whose records are available to us and whose studies have been completed.

We have no data to determine the proportion of cases of eczematoid dermatitis in which food sensitivity is the primary etiologic factor. It is our impression, however, that similar eruptions not responding to usual therapy (except roentgen irradiation) in three or four weeks have a definite food allergy factor.

Failure to recognize the primary importance of food allergy in these cases in the past has been due to a number of causes. 1. Cutaneous testing is not dependable. The only way to discover the offending foods is to test them by ingestion under careful supervision. 2. Prompt temporary improvement with roentgen ray therapy leads one to use this easy means of satisfying the patient. 3. The condition may be thoroughly disguised when first seen. Some patients have a superimposed pyogenic infection. The fundamental allergic factor cannot be discovered until

the superimposed picture is cleared. Local application of potassium permanganate soaks, débridement, use of weak ammoniated mercury ointment, sulfonamide compounds given internally and penicillin administered intramuscularly have been the best methods of accomplishing this. Some patients come into the hospital with superimposed dermatophytosis, which

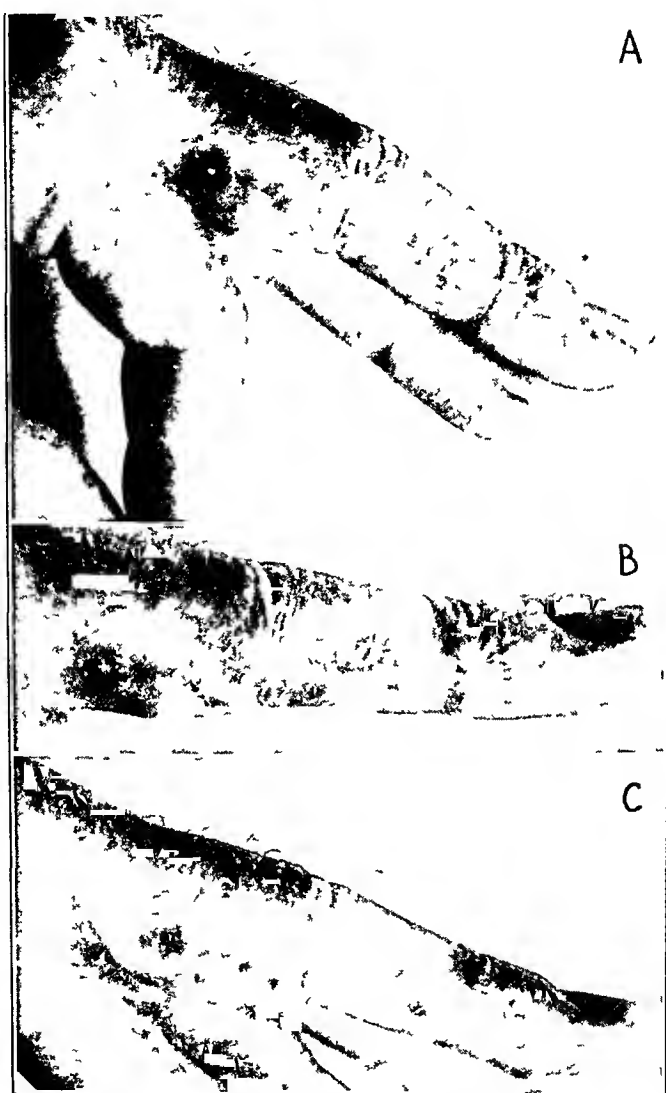


Fig 4 (case 9) —*A*, an acute vesicular flare-up twelve hours after pork was ingested. Prior to this the finger showed only some residual scaling.

*B* and *C*, subsiding of the flare in twenty-four and forty-eight hours. Note the disappearance of the tense vesicles and erythema and the general drying and scaling of the skin in twenty-four and forty-eight hours.

must be eliminated before a procedure can be adopted. 4 Food sensitivity, like every other allergy, is a complicated response which may vary from time to time, depending on fatigue, emotional states and cumulative

effects of many allergens. Moreover, new sensitivities may develop which complicate the picture.

Thus there are many pitfalls in the path of the sleuth who is on the trail of the malefactors. The process of following the clues and arriving at a complete understanding of the case takes a good deal of time. There

*Foods Which Have Caused Exacerbations of Dermatitis*

Food	Case No												
	1	2	3	4	5	6	7	8	9	10	11	12	13
Potatoes						+							
Beef													
String beans			+		+					+			
Coffee												+	
Milk			+	+		+	+						
Butter		+				+		+					
Bread	+	+				+		+					
Corn													+
Peaches	+								+	+			
Cream of Wheat	+	+				+		+					
Tea													
Chicken													
Eggs	+		+		+	+		+		+			
Spinach			+										
Rice	+												+
Orange juice					+								
Pineapple and pineapple juice	+		+		+		+						
Peas	+	+											
Tuna fish		+			+	+			+				
Cabbage								+					
Oatmeal													
Tomatoes and tomato juice		+	+		+				+	+			
Beets	+				+		+						
Cheese	+		+		+		+	+	+				
Cucumbers			+	+				nt	nt	nt			
Pork	+				+	+	+	+	+	+			
Salmon													
Peanut butter				+			nt	+					
Applesauce				+									
Grapefruit and grape fruit juice					+								+
Prunes								nt	nt	nt			
Cherries										nt			
Asparagus		+	+	+	+	+	nt	nt					
Baked beans		+	+		+					nt			
Onions								nt	nt	nt			
Carrots													
Sauerkraut							nt			nt			
Pears													
Chocolate						+	+	+	+				+
Raisins										nt			
Lemonade					+			+					
Beer	nt	nt	nt	nt	nt	nt	nt	nt	nt	nt	+	nt	nt
Sweet potatoes													
Lettuce													

The abbreviation "nt" indicates "not tested"

is no short cut. Roentgen ray therapy should not be used except for the residual changes after the allergens have been detected.

However, when the methods which we have outlined are followed the results are striking. Exacerbations usually occur within twelve hours, and always within twenty-four hours, after the patient has eaten an offending food. The mild reactions clear in thirty-six hours, the severer flare-ups accompanied with weeping of the patch subside within

four days The food factors can be recognized by the relatively rapid improvement which follows their elimination and by the prompt exacerbation which follows their ingestion The photographs (figs 1, 2, 3 and 4) show the changes which occur

There is a considerable likelihood that a larger series of cases will demonstrate that certain foods, particularly pork, cheese, eggs, wheat, and milk, are common offenders and that certain others, such as potatoes, beef, corn, tea and chicken, are less frequently responsible for eczematoid dermatitis The table shows the wide varieties of foodstuffs which have been demonstrated to cause unmistakable exacerbations of eczematoid dermatitis in our 13 cases None of the patients whose data are given in this table were sensitive to beef, chicken, oatmeal, tea and carrots Yet at the present time we have patients who are undergoing testing who have reacted definitely to each of these substances Further study may well show that there is no food to which some patient will not be sensitive Consequently, each food must be tested methodically to secure results <sup>4</sup>

#### SUMMARY

In 13 cases of eczematoid dermatitis food sensitivity was demonstrated to be the primary etiologic factor

The most satisfactory method of discovering the offending foods is by careful trial diets

Exacerbation and remission of the lesions follow promptly on administration and elimination of allergenic foods, so that the results of testing can be evaluated readily

Pyogenic and trichophytic infections are often superimposed on the underlying food sensitivity dermatitis They must be recognized and eliminated before food testing can be interpreted

There is probably no food which can be accepted as incapable of producing eczematoid dermatitis All must be tested methodically to secure results

During the preparation of the manuscript, valuable suggestions were rendered by Col Francis Wood, Medical Corps, Army of the United States

4 Adequate survey of the literature was not possible, since this work was done in an overseas theater A more complete review of the literature appears in a second article (Flood, J M, and Perry, D J Recurrent Vesicular Eruption of the Hands Due to Food Allergy, *J Invest Dermat* 7 309-327 [Dec ] 1946)

# BASAL SQUAMOUS CELL EPITHELIOMA ASSOCIATED WITH LEUKEMIA

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THE FIRST authentic case of the simultaneous occurrence of malignant disease and leukemia was described by Whipple in 1878. A total of 21 cases of combined leukemia and malignant growths had been reported up to 1944, according to Morrison, Feldman and Samwick.<sup>1</sup> All the malignant growths involved internal organs except those in the cases of Fuhs,<sup>2</sup> Scheufler<sup>3</sup> and Schreiner and Wehr,<sup>4</sup> who described epitheliomas of the skin. While Schreiner and Wehr described a case of epithelioma of the ear, associated with chronic lymphatic leukemia, originating on a normal skin, the epitheliomas described by Fuhs and Scheufler developed on a leukemid. Besides these reports, Schreiner and Wehr had, among 11,212 cases of malignant disease, an additional 4 cases. Since the association of leukemia with malignant growth, particularly the combination with cancer of the skin, is rare, we deemed it to be of sufficient interest to report the following case.

## REPORT OF A CASE

A white woman aged 61 years, was admitted in November 1944 to the Montefiore Hospital, with generalized lymphadenopathy. This had begun about two years previously, when she noticed a painless swelling of the posterior and anterior cervical glands. This was followed by a gradual enlargement of the axillary, epitrochlear and inguinal lymph nodes. About three years previously a small pustule appeared around the outer margin of the right eyebrow. Two similar lesions developed later, one below the right mandible and another on the right

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1 Morrison, M., Feldman, F., and Samwick, A. A. Carcinoma and Leukemia. Report of Two Cases with Combined Lesions, Review of Literature, *Ann Int Med* 20:75, 1944.

2 Fuhs, H. Multizentrisches Basalzellenepitheliom bei lymphatischer Leukemie, *Dermat Wchnschr* 85:1533, 1927.

3 Scheufler, A. Carcinombildung auf einem Leukämied, *Arch f Dermat u Syph* 168:586, 1933.

4 Schreiner, B. F., and Wehr, W. H. Cancer Associated with Leukemia, *Am J Cancer* 21:368, 1934.

side of the neck. All these lesions discharged, became crusted and refused to heal. Prior to admission the patient received, on account of severe anemia, several blood transfusions. On admission, Nov. 28, 1944, the patient revealed a generalized, discrete enlargement of lymph nodes. Bordering the outer margin of the



Fig. 1—Epitheliomatous lesions on the outer border of the right eyebrow and right side of the neck.

right eyebrow, there was an oval, flat, slightly infiltrated, eroded and crusted lesion, the border of which was slightly raised. Similar, but smaller, lesions were present above the lower mandibular margin on the right side and about in the center of the neck, corresponding to the lateral border of the sternocleidomastoid muscle.

*Blood Cell Counts in the Case Reported*

Date	Hemoglobin Gm	Red Blood Cells	Leukoocytes	Polymorpho nuclears, %	Lympho blasts %	Lympho cytes %
11/29/44	5.2	1,520,000	22,800	2	26	72
12/4/44	8.2	3,050,000	25,300	8	25	67
12/13/44	9.2	3,410,000	23,000			
12/18/44	10.5	3,800,000	28,000			
1/1/45	10.2	3,890,000	6,400	8	?	89
1/15/45	8.8	2,900,000	2,850		3	90
1/20/45	9.5	4,000,000	2,150			

The heart and lungs were essentially normal. Except for a moderate enlargement of the spleen, the abdomen did not disclose any abnormalities.

The blood cell counts in this case are given in the table.

Sternal puncture disclosed the following division of cells: myeloblasts 0.25 per cent, promyeloblasts 0.25 per cent, neutrophil myelocytes 4 per cent, nonsegmented neutrophils 1.75 per cent, segmented neutrophils 0.75 per cent, total myeloid series 7 per cent, lymphoblasts 92.25 per cent and normoblasts 0.75 per cent.

The patient received several blood transfusions, which caused temporary improvement in her blood picture. During the course of these hematologic examinations high voltage roentgen ray treatment was given to the entire body, which accounts for the depression of the leukocyte count.



Fig. 2—Basal-prickle cell epithelioma with horny pearl formation

A biopsy specimen of the cervical lymph node showed complete obliteration of the normal cellular architecture by a diffuse overgrowth of closely packed lymphocytes. The capsule was also invaded. These changes are compatible with malignant lymphatic lymphoma. The histopathologic changes in the section of the eroded lesions were as follows: In the corium beneath a superficial ulcerated epidermis there were many irregular, branching and anastomosing masses of epidermoid cells. These were fairly large, polyhedral and spindle shaped, the center and frequently columnar at the periphery. They had large vesicular and hyperchromatic nuclei, occasionally with large nucleoli. A few mitotic figures

were seen. Though a few pearls were present, the growth was essentially of the basal cell type, it originated, in many places, from the basal cells. There were considerable fibrosis in the corium, edema and hemorrhage. In addition to the carcinomatous process, a dense infiltration of lymphocytes in the corium and subcutaneous tissue which surrounded the carcinomatous tissue cells was present. While in one spot of the section indication was present of a possible relationship of this tumor with a lanugo hair, the invasive character, the size and the clinical character of the lesions were rather characteristic of a basal-spindle cell epithelioma of the skin with lymphocytic infiltration.



Fig. 3—Dense lymphocytic infiltration adjacent to the epitheliomatous proliferation

#### COMMENT

While the incidence of leukemia is not uncommon, the association with carcinoma belongs to the rarities. If one assumes that past observations are correct, a histogenetic relationship between leukemia and carcinoma does not appear probable. The circumstances concerning the relationship between leukemia and sarcoma, which may exist, have a different significance. It seems probable that both diseases are the exteriorization of the same virus. Sternberg<sup>5</sup> was the first who drew our attention to such cases, and he called it "leukosarcomatosis." On the basis of the experiments carried out by Oberling and Guérin,<sup>6</sup> it

5 Sternberg, C. Zur Kenntniss des Chloroms, Beitr. z. path. Anat. u. z. allg. Path. **37** 437, 1905.

6 Oberling, C., and Guérin, M. Les rapports entre leucémie et cancer à la lumière de recherches expérimentales récentes, Paris med. **1** 239, 1934.

does not seem impossible that a histogenetic relationship between leukemia and carcinoma may exist. These authors observed that the virus of chicken leukemia, after several passages through animals, may produce at the site of inoculation various types of tumors, such as spindle cell sarcoma, mycosis fungoides type of tumor or Rous sarcoma, and at times a prickle cell epithelioma may develop at the borders of a sarcoma. On the basis of their experiments, Oberling and Guérin refuted the hypothesis that the combination of sarcoma and epithelioma is coincidental, since they have succeeded in developing, in 2 instances, chicken epithelioma and sarcoma adjacent to each other from the leukemia virus. From such scanty evidence, it is too early to apply these observations to the histogenesis of human carcinoma from leukemia. It may, however, be of interest to devote future attention to such a remote possibility.

#### SUMMARY

1 A brief review of reported cases of cutaneous epithelioma and leukemia is given.

2 A case of a basal-prickle cell epithelioma of the skin in a woman with chronic lymphatic leukemia is presented.

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## USE OF TRICHOPHYTIN IN THROMBOANGIITIS OBLITERANS

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THE RELATIONSHIP of trichophytosis and peripheral vascular disease has been discussed by various authors<sup>1</sup> Studies<sup>1a</sup> were made which showed that a high percentage (93 per cent) of patients with thromboangitis obliterans had clinical trichophytosis while only 73 per cent of the controls had clinical trichophytosis Naide<sup>1a</sup> showed that four times as many patients with thromboangitis obliterans gave positive cutaneous reactions to trichophytin as those without the disorder Migratory phlebitis as a result of trichophytosis is well known, and "vascular trichophytids"<sup>2</sup> are also recognized

As far as I can find, the use of trichophytin in the treatment of thromboangitis obliterans or migratory phlebitis has not been carried on to any extent During the last year, I have seen 2 patients with thromboangitis obliterans whose response following the use of trichophytin was so dramatic that I feel that some attention should be given again to the possibility of the use of trichophytin as a therapeutic agent in this disease

### REPORT OF CASES

CASE 1—Mr I H, a Jewish man aged 36, who had had typical thromboangitis obliterans for six years, was seen March 15, 1945 because of severe urticaria In addition to the urticaria, he had a vesicular eruption on the hands and some scaling between the toes He was given 2 per cent iodine crystals in benzene to use on the feet Because of the possibility of a trichophytid, I made a trichophytin test In forty-eight hours he reported an erythematous, edematous reaction about 5 by 8 cm and tender I saw him again on March 18, 1945 The urticaria was about the same, but he remarked, "I don't know what you did to me the other day, but my feet are warm and comfortable for the first time in three or four years" The urticaria became so severe and the patient so mentally upset that he was hospitalized for about three weeks In the meantime, the urticaria was controlled and the patient returned to work

In July 1945 he had a recurrence of the symptoms of thromboangitis obliterans and returned to his internist He was sent to a surgeon for an examination for

1 (a) Naide, M The Causative Relationship of Dermatophytosis to Thromboangitis Obliterans, *Am J M Sc* **202** 822 (Dec) 1941 (b) Thompson, K. W The Relationship of Dermatomycoses to Certain Peripheral Vascular Infections *Internat Clin* **2** 156 (June) 1941

2 Peck, I Symposium on Allergic Dermatoses, *J Allergy* **11** 308 (March) 1940

possible surgical intervention to relieve his symptoms. The surgeon did not feel that operation was indicated. At the suggestion of the surgeon and the internist the patient returned to me, and I gave him trichophytin in a dilution of 1:240 once a week for four weeks and then trichophytin 1:120 once a week for four weeks. He was relieved of all symptoms of thromboangitis obliterans after the second week of treatment, and he has remained so.

CASE 2—Mr. F. W., aged 46, came to me Sept. 13, 1945, complaining of a scaling, vesicular eruption on the hands of six months' duration. In addition, he said that he had had thromboangitis obliterans for about four years and that during the last year had been unable to walk without a cane because of the severe pain in his legs. His feet had been constantly cold, and the great toe on his right foot had been exceedingly painful. He had received various types of treatment for the thromboangitis obliterans, without any appreciable relief.

I made a trichophytin test, using trichophytin in a dilution of 1:30, and after forty-eight hours he reported the presence of a wheal the size of a silver dollar. He was seen on Sept. 20, 1945. At this time he walked in without a cane and reported that he had little pain in the leg. He has since been given trichophytin in a dilution of 1:240 once a week, and now he is completely free of all pain. Only a slight discoloration of the toes appears when the feet are in a dependent position.

#### SUMMARY

Two patients with a trichophytid of the hands and thromboangitis obliterans were seen. These patients had clinical trichophytosis, the treatment of which had not influenced the vascular lesions. One patient (I. H.) had treated his feet from April to July, and they were clinically free of all infection, yet the symptoms of the thromboangitis obliterans were not affected. These patients were treated with trichophytin. The improvement both objective and subjective was rapid and decided. It is suggested that, in some patients with thromboangitis obliterans at least part of the inflammatory mechanism is initiated by an allergic reaction to the products of fungi and that trichophytin be given a more thorough trial as a therapeutic agent.

## CARDIOLIPIN-LECITHIN ANTIGEN

Recent Development Toward a Single Standard Test of the Blood for Syphilis

B S KLINE, M D  
CLEVELAND

**E**SSENTIALLY chemically pure cardiolipin-lecithin antigen, isolated by Pangborn and reported in 1941,<sup>1</sup> has been found to give more specific results in the microscopic slide precipitation test in nonsyphilitic patients than Eagle, Hinton, Kahn, Kline and Mazzini antigens and more sensitive results in patients with syphilis than Hinton, Kahn and Kline antigens<sup>2</sup>

The excellent results obtained with cardiolipin-lecithin antigen and the great simplicity of the slide flocculation technic recommend the two as a base for a single standard test of the blood for syphilis worthy of universal adoption (fig 1)

The simplification of technic from complex, time-consuming complement fixation tests for syphilis, requiring four reagents, to comparatively simple rapid flocculation tests, requiring but one, has been of great benefit to all concerned with the serodiagnosis of the disease

The most recently developed flocculation tests for syphilis are based on a mixture of the ingredients on an open slide. The slide tests are easier to perform and to read accurately and are more economical of time, material and space than are the tube tests

A measure of the interest in the slide flocculation tests is the fact that of thirty tests of the blood for syphilis evaluated at the recent Washington Serology Conference<sup>3</sup> twelve were slide flocculation tests. Nine of the tests evaluated were tube flocculation tests, and nine were complement fixation tests

From the Laboratory Department, Mount Sinai Hospital

Read before the Section on Dermatology and Syphilology at the Ninety-Fifth Annual Session of the American Medical Association, San Francisco, July 4, 1946

1 Pangborn, M C. A New Serologically Active Phospholipid from Beef Heart, *Proc Soc Exper Biol & Med* **48** 484, 1941, Isolation and Purification of a Serologically Active Phospholipid from Beef Heart, *J Biol Chem* **143** 247, 1942, A Note on the Purification of Lecithin, *ibid* **137** 545, 1941

2 Kline, B S. Cardiolipin Antigen in the Microscopic Slide Precipitation Test for Syphilis, *Am J Clin Path* **16** 68, 1946

3 Parran, T, Hazen, H H, Mahoney, J F, Sanford, A H, Senear, F E, Simpson, W M, and Vonderlehr, R A. The Washington Serology Conference, *Ven Dis Inform* **23** 161, 1942

More important in the development of a single standard test of the blood for syphilis than the simplification of technic is the improvement in the quality of the antigen employed. The original phenolized saline extracts of organs of a syphilitic fetus or child or other tissues containing *Treponema pallidum*, employed in 1906,<sup>4</sup> were quickly superseded by alcoholic extracts of normal organs.<sup>5</sup> For the past thirty-five years, purified alcoholic extracts (usually of beef heart powder previously treated with ether or acetone or ethereal or alcoholic extracts fractionated by acetone and dissolved in alcohol)<sup>6</sup> have demonstrated their superiority

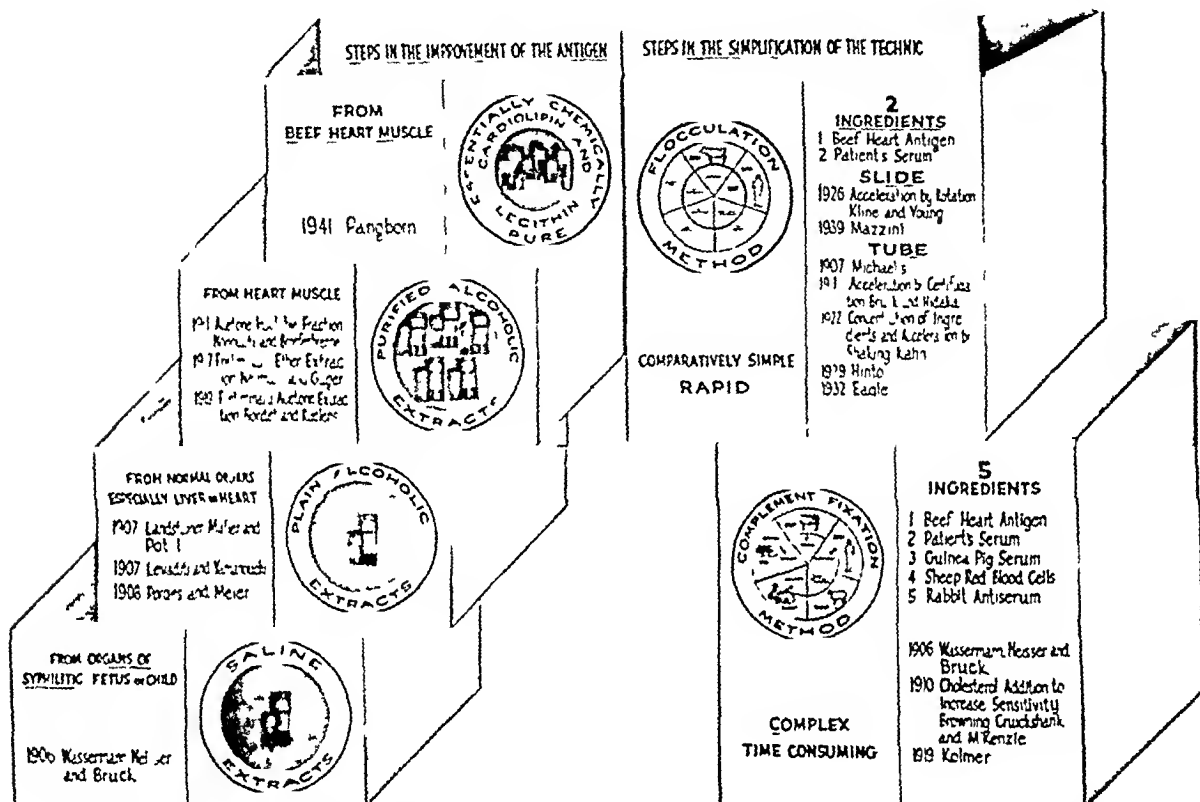


Fig 1—Steps in the improvement of the antigen and steps in the simplification of the technic for testing blood for syphilis

4 von Wassermann, A., Neisser, A., and Bruck, C. Eine serodiagnostische Reaktion bei Syphilis, *Deutsche med Wchnschr* 32 745, 1906

5 Landsteiner, K., Muller, R., and Potzl, O. Zur Frage der Komplement-bindungsreaktionen bei Syphilis, *Wien klin Wchnschr* 20 1565, 1907. Levaditi, C., and Yamanouchi, T. Le sero-diagnostic de la syphilis, *Compt rend Soc de biol* 63 740, 1907. Porges, O., and Meier, G. Ueber die Rolle der Lipide bei der Wassermannschen Syphilis-Reaktion, *Berl klin Wchnschr* 45:731, 1908

6 (a) Noguchi, H., and Bronfenbrenner, J. Biochemical Studies on So-Called Syphilis Antigen, *J Exper Med* 13 43, 1911. (b) Neymann, C. A., and Gager, L. T. A New Method for Making Wassermann Antigens from Normal Heart Tissue, *J Immunol* 2 573, 1917. (c) Bordet, J., and Ruelens, G. L'antigene syphilitique de l'Institut Pasteur a Bruxelles, *Compt rend Soc de biol* 82 880, 1919. (d) Kline, B. S. An Antigen for Use in Serum Tests for Syphilis, *J Lab & Clin Med* 13 588, 1928

over plain alcoholic extracts but nonetheless have been found to give nonspecific reactions, especially in cases of leprosy and malaria

As previously stated, Pangborn in 1941 reported the isolation from beef heart muscle of a previously unknown lipid and named it cardiolipin. She found that certain mixtures of this lipid and purified lecithin acted well as an antigen in a complement fixation test for syphilis. Since then, several reports of the value of cardiolipin-lecithin antigen in complement fixation and flocculation tests for syphilis have appeared.<sup>7</sup>

In a recent study,<sup>8</sup> cardiolipin-lecithin antigen was found to give more specific results in the microscopic slide precipitation test in non-syphilitic patients than Eagle, Hinton, Kahn, Kline and Mazzini antigens and more sensitive results in syphilitic patients than Hinton, Kahn and Kline antigen (tables 1, 2, 4 and 5 and fig. 2)

Table 1 shows the greater specificity of cardiolipin-lecithin antigen than that of Eagle, Hinton, Kahn, Kline and Mazzini antigens in cases of malaria. Table 2 shows the greater specificity in nonsyphilitic patients of optimal cardiolipin-lecithin mixtures than that of antigens containing comparatively large amounts of lecithin and a small amount of cardiolipin and than that of certain standard antigens.

Table 3 shows that in eight thousand, eight hundred and sixty-two consecutive tests of general hospital and ambulatory patients the specificity of optimal cardiolipin-lecithin antigen was greater than that of Kline antigen.

Table 4 shows that in the microscopic slide precipitation tests on syphilitic patients cardiolipin-lecithin antigen has greater sensitivity than the Hinton, Kahn and Kline antigens. In addition, it was found in tests of over six hundred and fifty serums in cases of syphilis that optimal cardiolipin-lecithin antigens gave more sensitive results than Kline antigen.

Figure 2 summarizes the comparative results of various cardiolipin-lecithin mixtures and Kline antigen in the microscopic slide precipitation test for syphilis and shows that mixtures of 1 part of cardiolipin and 94 and 106 parts of lecithin gave results of maximum specificity and of much greater sensitivity than did Kline antigen. In addition, it shows that mixtures of 1 part of cardiolipin and 117 or more parts

7 Brown, R. Cardiolipin, Lecithin, and Cholesterol in the Antigen in the Precipitation Test for Syphilis, *J. Bact.* **47** 581, 1944; Cardiolipin in Macro- and Microprecipitation Tests for Syphilis, *ibid.* **49** 199, 1945. Harris, A., and Portnoy, J. Cardiolipin Antigens in the Kolmer Complement Fixation Test for Syphilis, *Ven. Dis. Inform.* **25** 353, 1944. Maltaner, E., and Maltaner, F. The Standardization of Cardiolipin-Lecithin-Cholesterol Antigen in the Complement-Fixation Test for Syphilis, *J. Bact.* **49** 199, 1945. Rein, C. R., and Bossak, H. N. Cardiolipin Antigens in the Serodiagnosis of Syphilis. Microflocculation Slide Test, *Am. J. Syph., Gonorr. & Ven. Dis.* **30** 40, 1946.

Reaction	False Reactions		Total Tests	Total Reaction	False Reactions		Total Reaction	Total Tests	False Reactions	Total Reaction
	±	+			±	+				
7	1	11	101	108	1	11	101	108	1	11
2	2	9	11	108	2	9	11	108	2	9
3	3	9	11	108	3	9	11	108	3	9
4	4	9	11	108	4	9	11	108	4	9
5	5	9	11	108	5	9	11	108	5	9
6	6	9	11	108	6	9	11	108	6	9
7	7	9	11	108	7	9	11	108	7	9
8	8	9	11	108	8	9	11	108	8	9
9	9	9	11	108	9	9	11	108	9	9
10	10	9	11	108	10	9	11	108	10	9
11	11	9	11	108	11	9	11	108	11	9
12	12	9	11	108	12	9	11	108	12	9
13	13	9	11	108	13	9	11	108	13	9
14	14	9	11	108	14	9	11	108	14	9
15	15	9	11	108	15	9	11	108	15	9
16	16	9	11	108	16	9	11	108	16	9
17	17	9	11	108	17	9	11	108	17	9
18	18	9	11	108	18	9	11	108	18	9
19	19	9	11	108	19	9	11	108	19	9
20	20	9	11	108	20	9	11	108	20	9
21	21	9	11	108	21	9	11	108	21	9
22	22	9	11	108	22	9	11	108	22	9
23	23	9	11	108	23	9	11	108	23	9
24	24	9	11	108	24	9	11	108	24	9
25	25	9	11	108	25	9	11	108	25	9
26	26	9	11	108	26	9	11	108	26	9
27	27	9	11	108	27	9	11	108	27	9
28	28	9	11	108	28	9	11	108	28	9
29	29	9	11	108	29	9	11	108	29	9
30	30	9	11	108	30	9	11	108	30	9
31	31	9	11	108	31	9	11	108	31	9
32	32	9	11	108	32	9	11	108	32	9
33	33	9	11	108	33	9	11	108	33	9
34	34	9	11	108	34	9	11	108	34	9
35	35	9	11	108	35	9	11	108	35	9
36	36	9	11	108	36	9	11	108	36	9
37	37	9	11	108	37	9	11	108	37	9
38	38	9	11	108	38	9	11	108	38	9
39	39	9	11	108	39	9	11	108	39	9
40	40	9	11	108	40	9	11	108	40	9
41	41	9	11	108	41	9	11	108	41	9
42	42	9	11	108	42	9	11	108</		

[illegible]

Antigen	Room Temperature			Total Tests	1 to 20			Total	Room Temperature
	—	±	+		—	±	+		
1	50	0	0	50	1	2	1	20	178
2	10	1	0		1	1	1	20	178
3	10	1	0		1	1	1	20	178
4	10	1	0	50	1	2	1	20	178
5	10	1	0		1	1	1	20	178
6	10	1	0		1	1	1	20	178
7	10	1	0	50	1	2	1	20	178
8	10	1	0		1	1	1	20	178
9	10	1	0		1	1	1	20	178
10	10	1	0	50	1	2	1	20	178
11	10	1	0		1	1	1	20	178
12	10	1	0		1	1	1	20	178
13	10	1	0	50	1	2	1	20	178
14	10	1	0		1	1	1	20	178
15	10	1	0		1	1	1	20	178
16	10	1	0	50	1	2	1	20	178
17	10	1	0		1	1	1	20	178
18	10	1	0		1	1	1	20	178
19	10	1	0	50	1	2	1	20	178
20	10	1	0		1	1	1	20	178
21	10	1	0		1	1	1	20	178
22	10	1	0	50	1	2	1	20	178
23	10	1	0		1	1	1	20	178
24	10	1	0		1	1	1	20	178
25	10	1	0	50	1	2	1	20	178
26	10	1	0		1	1	1	20	178
27	10	1	0		1	1	1	20	178
28	10	1	0	50	1	2	1	20	178
29	10	1	0		1	1	1	20	178
30	10	1	0		1	1	1	20	178
31	10	1	0	50	1	2	1	20	178
32	10	1	0		1	1	1	20	178
33	10	1	0		1	1	1	20	178
34	10	1	0	50	1	2	1	20	178
35	10	1	0		1	1	1	20	178
36	10	1	0		1	1	1	20	178
37	10	1	0	50	1	2	1	20	178
38	10	1	0		1	1	1	20	178
39	10	1	0		1	1	1	20	178
40	10	1	0	50	1	2	1	20	178
41	10	1	0		1	1	1	20	178
42	10	1	0		1	1	1	20	178
43	10	1	0	50	1	2	1	20	178
44	10	1	0		1	1	1	20	178
45	10	1	0		1	1	1	20	178
46	10	1	0	50	1	2	1	20	178
47	10	1	0		1	1	1	20	178
48	10	1	0		1	1	1	20	178
49	10	1	0	50	1	2	1	20	178
50	10	1	0		1	1	1	20	178</

Various Antigens in Nonsyphilitic Patients (Centrifuged Emulsions)																
	Room Temperature			Total Tests	1 to 20			Total Tests	Room Temperature			Total Tests	Room Temperature			Total Tests
	-	±	+		-	±	+		-	±	+		-	±	+	
Angle	50	0	0	50	36	1	1	38	53	0	0	53	38	0	0	38
Hinton	50	1	0	50	37	1	1	38	53	0	0	53	38	0	0	38
Kahn	50	0	0	50	38	0	0	38	53	0	0	53	38	0	0	38
Kline	50	0	0	50	38	0	0	38	53	0	0	53	38	0	0	38
Maazini	50	0	1	50	34	3	1	38	53	0	0	53	38	0	0	38
Pangborn, 1 (cardiolipin)	50	0	0	50	17	0	0	17	53	0	0	53	38	0	0	38
Pangborn, 1 (cardiolipin)	50	0	0	50	36	1	1	38	53	0	0	53	38	0	0	38
Pangborn, 1 (cardiolipin)	50	0	0	50	37	1	1	38	53	0	0	53	38	0	0	38
Pangborn, 1 (cardiolipin)	50	0	0	50	38	0	0	38	53	0	0	53	38	0	0	38
Pangborn, 1 (cardiolipin)	50	0	0	50	34	3	1	38	53	0	0	53	38	0	0	38
Pangborn, 1 (cardiolipin)	50	0	0	50	17	0	0	17	53	0	0	53	38	0	0	38
Angle	50	0	0	50	36	1	1	38	53	0	0	53	38	0	0	38
Hinton	50	1	0	50	37	1	1	38	53	0	0	53	38	0	0	38
Kahn	50	0	0	50	38	0	0	38	53	0	0	53	38	0	0	38
Kline	50	0	0	50	38	0	0	38	53	0	0	53	38	0	0	38
Maazini	50	0	1	50	34	3	1	38	53	0	0	53	38	0	0	38
Pangborn, 1 (cardiolipin)	50	0	0	50	17	0	0	17	53	0	0	53	38	0	0	38
Pangborn, 1 (cardiolipin)	50	0	0	50	36	1	1	38	53	0	0	53	38	0	0	38
Pangborn, 1 (cardiolipin)	50	0	0	50	37	1	1	38	53	0	0	53	38	0	0	38
Pangborn, 1 (cardiolipin)	50	0	0	50	38	0	0	38	53	0	0	53	38	0	0	38
Pangborn, 1 (cardiolipin)	50	0	0	50	34	3	1	38	53	0	0	53	38	0	0	38
Pangborn, 1 (cardiolipin)	50	0	0	50	17	0	0	17	53	0	0	53	38	0	0	38
* F D indicates fine dispersion and O D, coarse dispersion, -, ± indicates between - and ±																

of lecithin gave positive reactions in nonsyphilitic patients and are therefore unsatisfactory for use

TABLE 3—Positive Reactions in Slide Tests with Cardiohupin-Lecithin and Kline Antigens in General Hospital and Ambulatory Patients with No Evidence of Syphilis

Antigen	Total Tests (6/26/45 to 5/15/46)	± Weakly Positive	Positive Reactions	
			%	+ Positive
Cardiolipin lecithin	8,862 *	11 †	0.12	5 †
Kline	8,862 *	30	0.34	27

\* Includes cases with data insufficient for evaluation

† In 3 cases of uterine fibroids the reactions were weakly positive, and in 2 cases they were positive. Two patients with diabetes mellitus gave a weakly positive reaction, and 1 gave a positive reaction. In 2 cases of pregnancy the reactions were weakly positive and in 1 case positive. In 4 patients with other conditions the reactions were weakly positive, in 1 the reaction was positive.

TABLE 4—Sensitivity of Various Antigens\* in Slide Tests in Cases of Syphilis

There were twenty one serums of low titer eliciting positive reactions with uncentrifuged emulsions, twenty one serums of low titer elicited positive reactions with centrifuged emulsions.

	—	±	+	Total Tests
Eagle	0	4	37	41
Hinton	6	10	24	40
Kahn	5	15	18	41
Kline	16	16	9	41
Mazzini	0	5	36	41
Pangborn, 1 (cardiolipin)	0	6	35	41
Pangborn, 2 (lecithin)	0	6	35	41

\* The various antigens employed in preparing slide test emulsions with identical quantities of water, cholesterol and salt solution were used in the following optimal amounts Mazzini, 0.075 cc Kline, 0.1 cc, cardiolipin, 0.1 cc, Eagle, 0.2 cc to 0.25 cc, Kahn, 0.25 cc to 0.3 cc, and Hinton, 0.2 to 0.25 cc

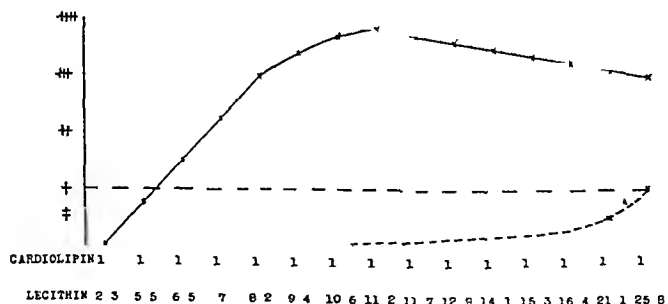


Fig 2—Sensitivity of the various mixtures of Pangborn cardiolipin and purified lecithin in slide tests as compared with that of standard slide test antigen on serums of low titer eliciting positive reactions (estimated on the basis of a 1 plus reaction in the standard diagnostic slide test). The continuous line indicates the specific reaction with uncentrifuged emulsions. The broken line indicates the nonspecific reaction with centrifuged emulsions. The broken line with dots indicates the reaction to the standard slide test with diagnostic emulsions.

That cardiolipin-lecithin antigen is not absolutely specific for syphilitic reagin is evidenced by the occurrence of occasional positive reactions in nonsyphilitic patients as shown in tables 1, 2 and 3, and in patients

Table 5—*Reactions of Kline and Cardiolipin Antigens in Serum of Lower Animals (Centrifuged Emulsions)*

	Horse			Beef			Sheep			Hogs			Dogs †		
	—	±	+	—	±	+	—	±	+	—	±	+	—	±	+
	Total Tests			Total Tests			Total Tests			Total Tests			Total Tests		
Kline	0	0	20	0	0	25	1	3	21	25	14	10	26	50	8
Pankhorn, 1 (cardiolipin) 10.6 (lecithin)	1	1	18	14	1	7	14	3	8	25	27	3	20	50*	12
Pankhorn, 1 (cardiolipin) 25.8 (lecithin)	1	1	18	6	9	10	11	1	10	25					

\* Cardiolipin antigens in tests of hog serum, contained 1 (cardiolipin) 6.5 (lecithin)

† The dog bloods were kindly furnished by Dr. H. Goldblatt, Institute of Pathology, Western Reserve University School of Medicine

with leprosy, as reported by Rein.<sup>7</sup> It has been pointed out also that results with optimal cardiolipin-lecithin antigen are not always reliable in tests with uterine blood and blood from the cord and with merthiolated serum.<sup>2</sup> Furthermore, positive reactions occur in tests of cardiolipin-lecithin antigen with horse, beef, sheep and hog blood serum.<sup>2</sup> (table 5)

In spite of these limitations of cardiolipin-lecithin antigen, the fact that it is composed of essentially chemically pure lipids makes it possible for the first time in the serodiagnosis of syphilis to obtain uniform results with lot after lot of antigen. Furthermore, the fact that cardiolipin-lecithin antigen in the microscopic slide precipitation test gives results of maximum sensitivity and at the same time more specific results than present day standard antigens indicates its great value in the serodiagnosis of syphilis and represents an important step toward the development of a single standard test of the blood for syphilis.

Future studies may reveal better methods of preparing antigen emulsions and better conditions for their use in a slide flocculation test than those employed today. Furthermore, an antigen more specific for syphilitic reagin than cardiolipin-lecithin antigen may be found.

#### SUMMARY

Essentially chemically pure cardiolipin-lecithin antigen, isolated by Pangborn and reported in 1941, has been found to give more specific results in the microscopic slide precipitation test in nonsyphilitic patients than Eagle, Hinton, Kahn, Kline and Mazzini antigens and more sensitive results in patients with syphilis than Hinton, Kahn and Kline antigens.

The excellent results obtained with cardiolipin-lecithin antigen and the great simplicity of the slide flocculation technic recommend the two as a base for a single standard test of the blood for syphilis worthy of universal adoption.

Mrs H. Suessenguth and Miss M. Stephens gave technical assistance, and Mrs. Suessenguth gave valuable suggestions concerning the manuscript.

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#### ABSTRACT OF DISCUSSION

DR. A. S. GIORDANO, South Bend, Ind. I am grateful for the opportunity of being here to pay tribute to Dr. Kline for the contribution that he has made to the serology of syphilis. It was he, some ten years ago, that initiated the study of purifying antigen by precipitating out, so to speak, all the unspecific or non-specific substances in the antigens that physicians were using. Today he is perhaps on the threshold to the realization of his dream.

About seven years ago, the American Society of Clinical Pathologists was convinced from his various studies that he presented that something should be

done to assist him in solving this problem. Accordingly, they appointed a committee to raise funds in order that well trained chemists could be obtained to complete this job. Today there is this new cardiolipin antigen that has performed as Dr Kline has described.

In our laboratory, my colleagues and I are running parallel series of studies, and we wish to substantiate everything he has said. So far the specificity is far superior to that of tests now in use. We were particularly using the Mazzini test. In our work we found that this test, even though highly desirable and sensitive, gave an uncomfortably high number of nonspecific reactions. In the National Serologic Conferences, many types of serums are not studied. I refer particularly to those in obstetric cases, general sepsis and various other types of infection.

In this group of patients we found the highest number of nonspecific reactions, and it made it extremely difficult for us to keep in touch with physicians to warn them that such a test in all probability might be false and they must use caution.

In the use of cardiolipin, serologists have practically done away with these nonspecific reactions. As Dr Kline thinks that there may be a better antigen, it may be true, but this one certainly, I believe, will replace all those that serologists have so far had opportunity to use.

DR M. H. MERRILL, Berkeley, Calif. Serologists are confronted with two basic problems. The first is the multiplicity of serologic tests for syphilis. The second is the varying levels of sensitivity and specificity from laboratory to laboratory of any given test procedure.

There are two basic serologic procedures—complement fixation and flocculation—and numerous applications of each of these. In California there are three hundred and five laboratories approved to do serologic tests for syphilis. A total of eight different tests are employed within these laboratories. As the problem is studied, varying degrees of deviations from the published procedures of the authors of these eight procedures are constantly being encountered, which multiplies the actual number of tests being used.

I mention these facts to indicate what an advance it might be if serologists could eventually arrive at a single easily standardized test procedure that would be used by all laboratories.

The second problem pertains to varying levels of sensitivity and specificity in any given test from laboratory to laboratory. It is in this category that it seems to me that the introduction of cardiolipin represents a real advance. For the first time it now appears to be within the grasp of serologists to have an antigen composed of pure chemical substances. Such an antigen can apparently actually be standardized without having to enclose the term in quotation marks. The development of this antigen may well remove one of the troublesome variables in serologic tests for syphilis. One is still, however, dealing with a delicately balanced biologic test. The purity of the salt solution, exact adjustment of salt concentration and purity of the alcohol used as the solvent are examples of other factors that must be considered. The greatest single variable heretofore has been the antigen itself. The essential control of the factor is therefore a genuine advance.

It must be recognized, however, that this antigen can be used in complement fixation tests as well as flocculation tests and also that it can be used in tube flocculation tests as well as slide microscopic flocculation tests. The battle of the tests will undoubtedly continue for some time even after cardiolipin antigen becomes readily available. Dr Kline has clearly demonstrated, it seems to me, that this new antigen possesses distinct advantages when the Kline microscopic slide technic

is applied. The workers in the New York State Laboratory are, I believe, equally convinced that it provides similar advantages when used in the complement fixation test. Workers who have used cardiolipin antigen, regardless of the procedure of the test, are apparently in agreement concerning its superiority. Apparently science has moved forward another step in the development of the serologic testing for syphilis. It is not inconceivable that as soon as it becomes available this antigen may be generally adopted.

For a number of years my colleagues and I have been using the Kline exclusion test in our California state laboratory. We have recognized that this test, as all serologic tests for syphilis, has some limitations. We welcome Dr. Kline's report on the use of this new antigen in his test. This will go far toward correcting some of the problems we have encountered. I congratulate Dr. Kline on this new application of a test procedure we have found most adaptable to large scale testing. Nevertheless, we are hardly yet prepared to say that we can eliminate other test procedures, particularly the complement fixation test. We shall want to run comparative studies on a significant series of specimens before considering the elimination of the complement fixation test, particularly on spinal fluids, on serums in cases of prenatal syphilis and for quantitative reagin determinations. I say this, hoping, however, that in the not too distant future we may be able to rely on one test and that all other laboratories in the state may do likewise. Dr. Kline's procedure may be that test, but we can hardly say as much at this time.

DR. R. C. ARNOLD. Pangborn has isolated the so-called cardiolipin in which the antigenic potential appears to be invested and which has been used in the preparation of antigens. Alone, cardiolipin has not been found to be suitable as an antigen in the present serodiagnostic techniques; its reactivity must be enhanced by lecithin and cholesterol. It is difficult to prepare such complex organic compounds in a pure chemical state, and the contiguous substances may interfere with reproducible antigenic activity. At present the proportionate ratio of the essential antigen components needs adjustment from lot to lot. Future developments in isolation and purification of the components may obviate the need for serologic standardizations of cardiolipin antigens. The parallel control of all components cannot be overemphasized.

An optimum combination of these substances may be used for antigenic purposes in a slide and tube precipitation test and in a complement fixation test. The level of sensitivity appears to be equal to or better than that obtained with the cruder lipid antigens. Also, some factors of nonspecificity may have been removed. The exact status of sensitivity and specificity will be determined by future laboratory and clinical evaluations.

Cardiolipin represents a definite advancement toward the ideal antigen for the serologic tests for syphilis and may well serve as the basis for the greatly needed standardization of serodiagnostic methods.

Research should be continued in the field of antigenic and supplementary substances so that the resulting antigens will be constant in character, reproducible in activity and adaptable to normal laboratory conditions. Consideration may be given toward the simplification and standardization of serologic tests to replace the numerous technical procedures, each of which now has multiple and ever-changing modifications.

In any discussion of serologic tests for syphilis, it is well to remember that the antigen, though of primary importance, is only one factor. Among others, the condition of the specimen, the other test reagents, the test technic and the method of performance all affect the results of the test. The indulgence and

cooperation of the physicians will be helpful during the laboratory and clinical evaluation of tests employing cardiolipin antigens, in the fields of both established syphilis and other diseases which may give nonspecific positive reactions

Dr Kline has arranged a most interesting display dramatizing the historical and educational highlights of his presentation. Either the display or the discussion would be sufficient to remind one of the rapid advances in scarcely forty years of serology in syphilis and to point, I believe, to even more rapid progress in the immediate future.

DR. GEORGE W. BINKLEY, Cleveland. Dr Kline has shown a satisfactory decrease in the number of nonspecific reactions when the cardiolipin antigen is used. In eight thousand, eight hundred and sixty-two routine serums for testing from presumably healthy donors, the Kline exclusion test gave about thirty positive reactions while the cardiolipin test gave only eleven positive reactions. This means much less unnecessary investigation for clinicians, not to mention anxiety for the patients. With the previously employed flocculation tests, the Kline, Kahn, Hinton, Eagle and others, there was an almost uniform 16 per cent false positive incidence in serums from patients with active malaria. With the cardiolipin antigen only 1 per cent false positive reactions were obtained.

We will await with great interest the results of serologic tests in other infections, such as leprosy, lymphogranuloma venereum, postvaccinal infection and infectious mononucleosis, with the cardiolipin antigen.

I believe that Dr Kline has not yet had the opportunity to make serologic tests in yaws, pinta or the spirochetal type of rat bite fever with this antigen. However, one should expect the cardiolipin to give positive results in these diseases because of the similarity of the reagin formed.

DR. CHARLES R. REIN, New York. Dr Kline is to be congratulated on the successful adaptation of a cardiolipin antigen to his microscopic slide flocculation test. He has selected a ratio of cardiolipin and lecithin (1:102) which he found to be optimal for his test. Ad Harris and his collaborators have also employed a cardiolipin-lecithin antigen (ratio 1:9) in a microfloculation test, with similar excellent results. At the Army Medical School my colleagues and I have used the cardiolipin-lecithin antigens in a microfloculation test (ratio 1:65) and in a complement fixation test (ratio 1:5). The sensitivity of our tests with cardiolipin antigens is definitely higher than that obtained with similar tests employing the routine standard lipid antigens. The specificity of these cardiolipin tests is also greatly improved, and it is especially evident in patients with malaria. Captain Kent and I presented a paper yesterday on our results in a series of volunteer nonsyphilitic prisoners with sporozoite-induced malaria. The unusual specificity of our cardiolipin microfloculation test in this group was striking.

Dr Mary Pangborn has made a most important contribution to medicine in her discovery and isolation of cardiolipin. The use of this purified substance has enabled serologists to improve the sensitivity and specificity of their tests for syphilis.

It should be pointed out, however, that the cardiolipin tests also have definite limitations in that false positive and false negative reactions may be obtained with them. In a series of 35 patients with leprosy the incidence of nonspecific (false positive) reactions was just as high with cardiolipin tests as with the routine tests in our serologic battery. In a few nonsyphilitic patients with infectious mononucleosis, the reactions in the cardiolipin tests were the first to become positive and the last to become negative when compared with reactions in a batter-

of six other tests I am certain that when these cardiolipin antigens are more widely used other nonsyphilitic diseases and conditions will be found that will produce false positive reactions

We have also had an opportunity to use cardiolipin tests in a series of blood specimens from patients with yaws and pinta As was expected, we obtained a high percentage of strongly positive reactions

CAPTAIN JOHN KENT, Washington, D C It appears from these adaptations that the microflocculation, precipitation and complement fixation procedures require different proportions of cardiolipin, lecithin and cholesterol as antigen However, the various modifications of each of these procedures require strikingly similar proportions of the constituents This similarity suggests the ultimate use of a standard cardiolipin antigen, for example, in all microflocculation methods Such standardization extended to precipitation and complement fixation tests would represent an important accomplishment, since it would make possible the evaluation of technics without consideration of antigen and permit perhaps the final selection of a single, optimal microflocculation, precipitation and complement fixation test from the many named variations in current use

## SULFONAMIDE PSORIASIFORM DERMATITIS

OSGOODE S. PHILPOTT, M.D.  
DENVER

IT IS WELL known that members of the sulfonamide group of drugs may produce untoward cutaneous reactions. Further reference to this fact may seem unnecessary, but I have observed during the last few years a cutaneous eruption due, I think, to sulfonamide compounds and not, to my knowledge, previously reported. This is a type of psoriasiform dermatitis, exhibiting many of the essential features of psoriasis, and in at least 1 of 4 cases may be true psoriasis.

Costello, Rubinowitz and Landy<sup>1</sup> reported twenty-nine dermatoses attributed to the local or internal use of sulfathiazole, but in this group there is no mention of any resembling psoriasis. The literature, while rich in references to a wide variety of sulfonamide dermatoses, does not include any of the type I wish to report in this paper.

My first contact with this interesting condition was in 1941, when a woman was seen in my office with an eruption which was apparently psoriasis. There was nothing unusual about the appearance of the cutaneous lesions, but I was startled by Dr. Markley's statement that he thought that the woman's psoriasis was due to sulfanilamide. Subsequent investigation seemed to bear out this observation, but unfortunately I did not have the opportunity for further study of the case. Later, when I encountered similar lesions in patients who had recently received sulfonamide drugs, the idea of reporting them crystallized. The majority of my patients were women, some I followed for three or more years, a number were seen only once, having been patients referred from out of town for diagnosis. From the cases in which the conditions were so diagnosed, 3 are here reported as illustrating some of the clinical features common to the entire group.

### REPORT OF CASES<sup>2</sup>

CASE 1—N. D., a white woman aged 18, was referred to my office for diagnosis and treatment. At this visit she stated that she had been well until two weeks previously, when there had developed an illness consisting of headache,

Read before the Section on Dermatology and Syphilology at the Ninety-Fifth Annual Session of the American Medical Association, San Francisco, July 5, 1946.

<sup>1</sup> Costello, M. J., Rubinowitz, A. M., and Landy, S. E. Sulfonamide Therapy in Dermatology, *New York State J. Med.* **42**: 2309-2317 (Dec. 15) 1942.

<sup>2</sup> From the private practice of Dr. A. J. Markley, Dr. O. S. Philpott and Dr. A. R. Woodburne.

fever, sore throat and generalized distress. Her physician prescribed 21 grains (1.5 Gm) of sulfathiazole every three hours for three days. Feeling better, she returned to work, and within a few days she noticed a "breaking out of small pimples" on the elbows, knees and scalp. The eruption spread rapidly over the extensor surfaces of the extremities and on the forehead, extending downward to the eyebrows. When first examined, most of the lesions were maculopapular, bright red and small and covered with white, adherent, dry scales. A diagnosis of acute psoriasis was made. Routine treatment was instituted, including auto-hemotherapy. The number of lesions increased, and the older lesions became progressively more papular and in places confluent. The patient was then hospitalized.

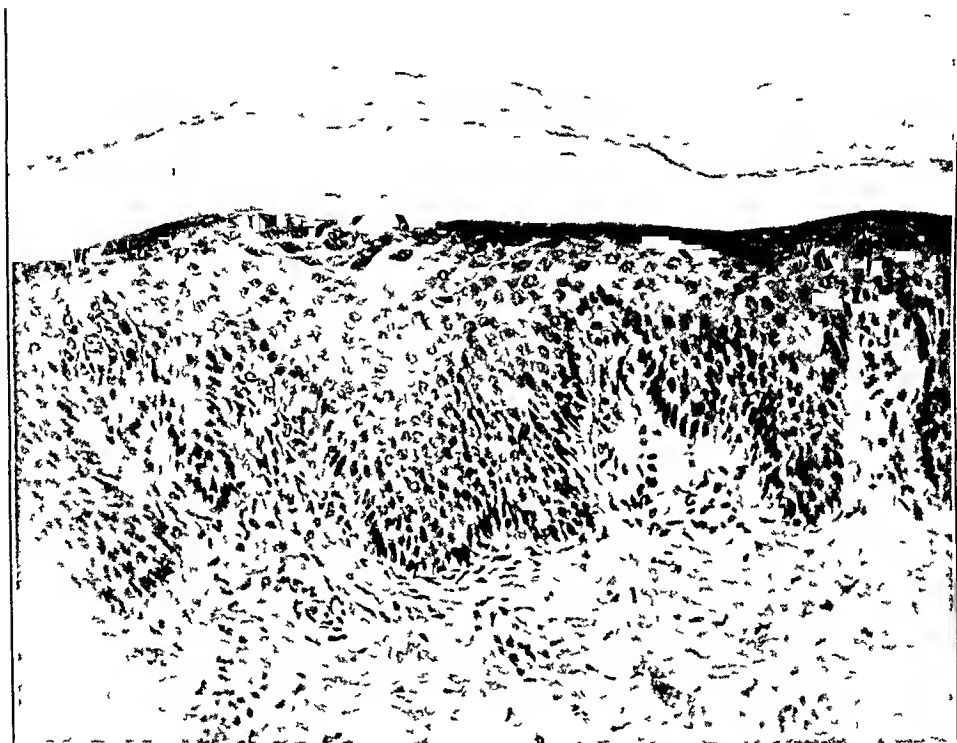


Fig 1 (case 1)—Epidermal cellular and nuclear changes and dermal lymphocytic infiltration consistent with the lesions of psoriasis  $\times 90$

*Hospital Digest*—Physical examination revealed a well nourished, well developed white woman appearing somewhat more mature than her stated age of 18. The skin revealed red, rounded, discrete, flat-topped papules, which were dry and usually covered by silvery scales. Where the lesions were thickest they tended to coalesce. They were found over the entire body and face, especially about the hair line, on the extensor surfaces of the arms and legs and about the elbows and knees. Wherever the patient had a scar on her body lesions developed.

*Physical Examination*—Physical examination showed normality with the exception of the aforementioned cutaneous lesions and hypertrophied tonsils. A roentgenogram of the chest was normal. The urine and blood cell count were normal. Other laboratory examinations, including studies of blood chemistry, gave normal

results. The serologic reaction of the blood was negative. A small piece of skin was removed partially from a typical lesion and partially from the adjacent normal skin for histologic examination.

*First Microscopic Examination* (fig 1)—Sections showed hyperkeratosis of the stratified squamous epithelium. The superficial cornified epithelium was thin and appeared shredded. The rete cones were elongated and broadened, with occasional formation of daughter rete pegs. The papillae were ballooned and in areas showed small collections of lymphocytes in the tips of the papillae. In the dermis were small collections of lymphocytes.

*Pathologic Diagnosis*—The pathologic diagnosis was chronic dermatitis, with lesions consistent with psoriasis.

*Therapy*—The patient received ultraviolet irradiation, petrolatum on the body and 10 per cent ammoniated mercury ointment on the scalp.

*Diagnosis*—The patient was discharged, with the diagnosis of psoriasis, unimproved.

*Course*—For the next few months the patient was treated at the office, and the eruption gradually improved until she was free of lesions on the glabrous skin. With the exception of scaling and redness on the scalp she remained clear for fifteen months, until she contracted an infection of the upper respiratory tract. During this sickness she noticed the appearance of small, red areas on both legs. These increased in size until many were 1 inch (2.5 cm) or more in size and irregularly shaped. All were moderately infiltrated and scaly. A second biopsy was performed at this time.

*Second Microscopic Examination*—Sections showed parakeratosis with desquamation of sheets of epithelium, often containing clear spaces. The papillary layer frequently approached the surface, was highly vascular and contained moderate numbers of lymphocytes. Lymphocytes were also prominent about the vessels in the deeper corium. A few of the epithelial cells of the prickle cell layer were vacuolated. The picture was suggestive of that seen in psoriasis but was not sufficiently so to make that diagnosis.

*Diagnosis*—The diagnosis was chronic dermatitis.

*CASE 2*—M. W., a white woman aged 30, examined at my office, had a great number of lesions over the entire body. The size of the lesions varied from  $\frac{1}{8}$  inch to 2 inches (0.32 to 5 cm). They were dull red, raised and scaly, with irregular outlines, but sharply margined. On the elbows and knees were thick, discoid patches, resembling either lichen simplex chronicus or chronic psoriasis (figs 2 and 3). The patient had had the eruption for about four months. The mucous membranes, palms and soles were not involved. There was no history of previous eruptions. There had been no psoriasis in her immediate forebears. She gave a history of an incident of "streptococcal infection" of the throat two months before I first examined her. She had taken sulfonamide drugs on several occasions, the last time being a few weeks before the eruption appeared. At this visit a diagnosis of chronic psoriasis (four months' duration) was made. Treatment was outlined and followed, without benefit. The patient was then hospitalized.

*Hospital Digest*—This 30 year old white woman entered the hospital with a history of onset of eruption across the shoulders five months previously. These cutaneous lesions were small, painless and pruritic. The lesions over the shoulders cleared up after a few days but reappeared on the legs. The areas on the legs became larger. The chief complaint was pruritus. The areas bled fairly easily.

The lesions spread progressively, and by the time of the patient's admission they had involved most of the skin of the body. Seven days prior to admission the lesions began to spread to the face. Lesions of the skin appeared first as small, red, nontender papules, which enlarged and spread. The remainder of the history was noncontributory.

*Physical Examination*—The temperature was 98.2 F, the pulse rate 84, the respiratory rate 20 and the blood pressure 122 systolic and 74 diastolic. The patient



Fig 2 (case 2)—Lesions on extensor surface of arm and elbow

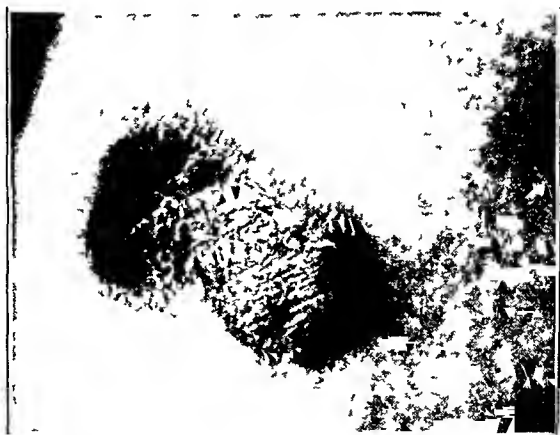


Fig 3 (case 2)—Closer, more detailed, view of the lesion of psoriasis

was a well developed, well nourished white woman, ambulatory and not in acute distress. The skin showed numerous widespread, dull red, well demarcated, circular, elevated, indurated, scaly lesions all over the body except for the hands and feet, the lesions varied from 2 or 3 mm to 4 or 5 cm in size. Several new small lesions were present on the face. The eyes, ears, nose and throat were essentially normal. The head and neck were normal except for cutaneous lesions. The lungs were clear to auscultation and percussion. The heart was

within normal limits. The abdomen was normal. The reflexes were physiologic. The impression was psoriasis.

*Laboratory Findings*—The picture on hematologic examination was within normal limits except for a somewhat increased total white cell count, the differential count being essentially normal. The sedimentation rate was normal. The blood chemistry was normal.

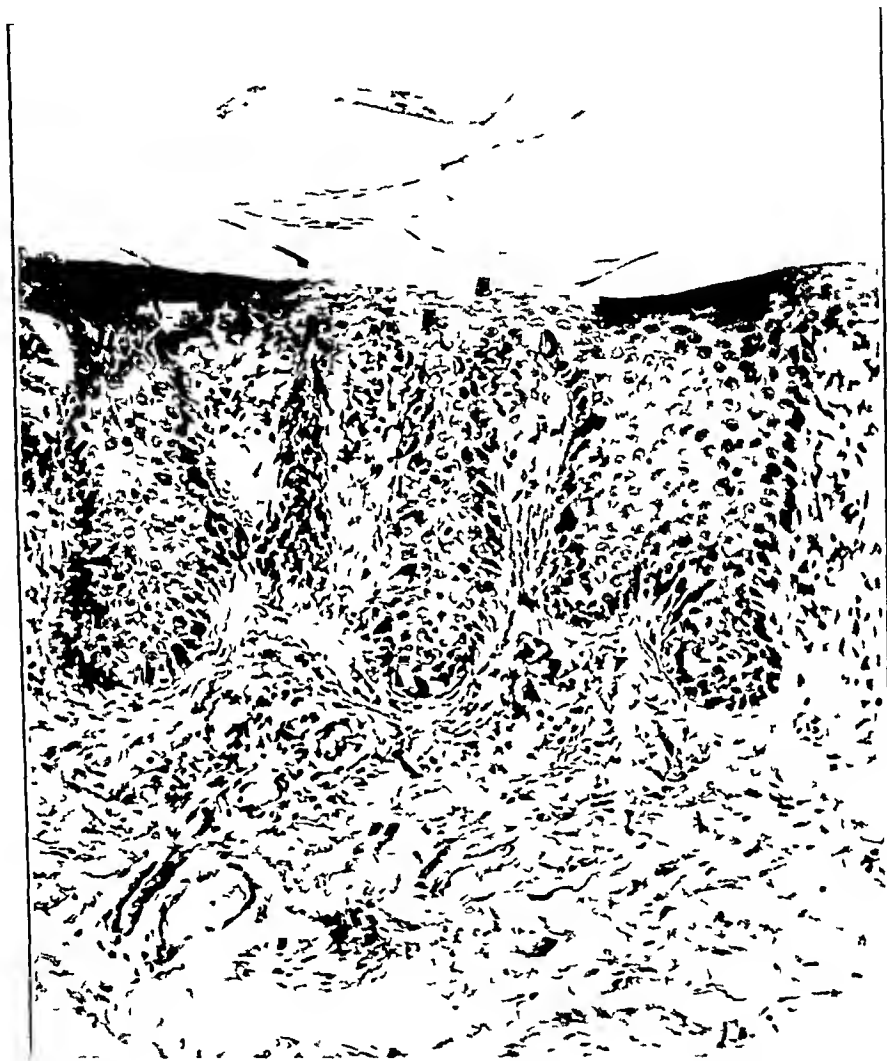


Fig 4 (case 2)—This section shows parakeratosis and cellular degeneration in the rete cells with intercellular edema  $\times 90$

*Microscopic Examination* (fig 4)—Sections showed the stratified squamous epithelium to be somewhat hyperplastic but otherwise normal. Just beneath the epithelium were areas of round cell infiltration.

*Pathologic Diagnosis*—The pathologic diagnosis was chronic dermatitis. It was believed that the throat was the source of infection, and a consultation for examination of the throat was requested. The diagnosis from this was chronic tonsillitis, with a recommendation for tonsillectomy, which was done. The patient's condition following this was good. Treatment directed to the psoriatic lesions for the remainder of the patient's stay in the hospital was application of a 3 per cent

crude coal tar ointment at night and ultraviolet irradiation in the morning. Much improvement in the lesions was noted, there was a softening and loss of the scaly appearance. However, the lesions did not wholly disappear. The patient was dismissed.

*Final Diagnosis*—The final diagnosis was psoriasis. The patient's condition was improved.

Following her episode in the hospital she had an occasional roentgen ray treatment. During the summer she followed a modified Goeckermann treatment, with indifferent results. Her elbows and knees have been continuously involved, although there were several weeks during the fall when the rest of her body was clear.

CASE 3—Y. C., a white girl aged 8 years, presented a symmetric eruption composed of a multitude of small, red, discrete macules. These were only slightly

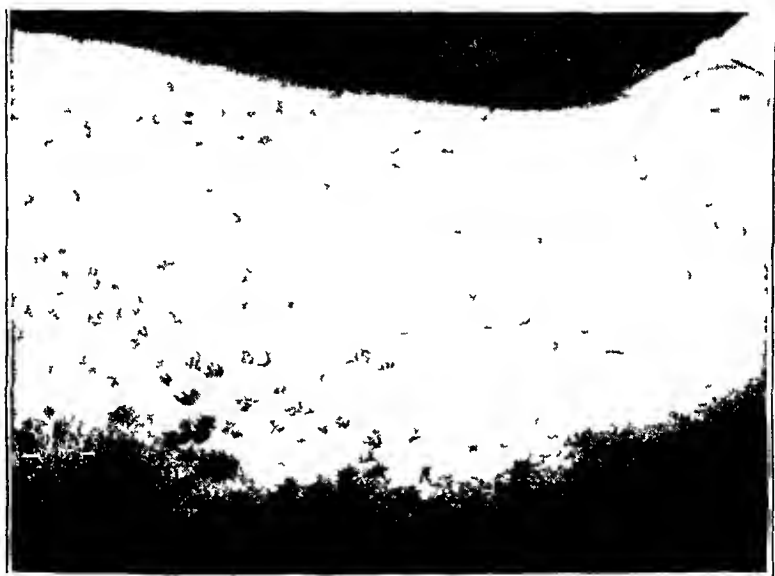


Fig 5 (case 3) —In this case nearly every lesion was of the same color, shape and papular stage of development.

scaly and just barely palpable. Nearly every lesion was about the same in size and outline and maintained about the same rate of development during the next few weeks when the majority were definitely papular and had white glistening scales (fig 5). The hands and feet and the part of the body above the shoulders escaped involvement. The greatest concentration of lesions occurred on the sides of the trunk, and about the umbilicus the papules were so thick they formed a confluent cast. The florid appearance and distribution and sudden development of this eruption justified a clinical diagnosis of acute psoriasis of the guttate variety. There was no familial history of psoriasis and no previous history of a cutaneous disease. The young patient had rheumatic fever and had been under close medical supervision for more than a year. She had taken 10 grains (0.65 Gm) of sulfanilamide daily for many weeks, and for some unexplained reason, this dose had been doubled a fortnight before I saw her. Two days later the eruption began. After this a typical lesion was removed from the right side of the lower part of the abdomen for pathologic study.

*Microscopic Examination* (fig 6)—The corneal layer was thin, the epidermis was thickened and the granular and germinal layers showed spongiosis and acanthosis. The granular and basal layers showed mitosis, and the rete pegs were elongated, as were the papillary bodies of the dermis, which showed perivascular infiltration.

*Pathologic Diagnosis*—The pathologic diagnosis was epithelial hyperplasia and chronic dermatitis, consistent with psoriasis. Under moderate treatment in con-

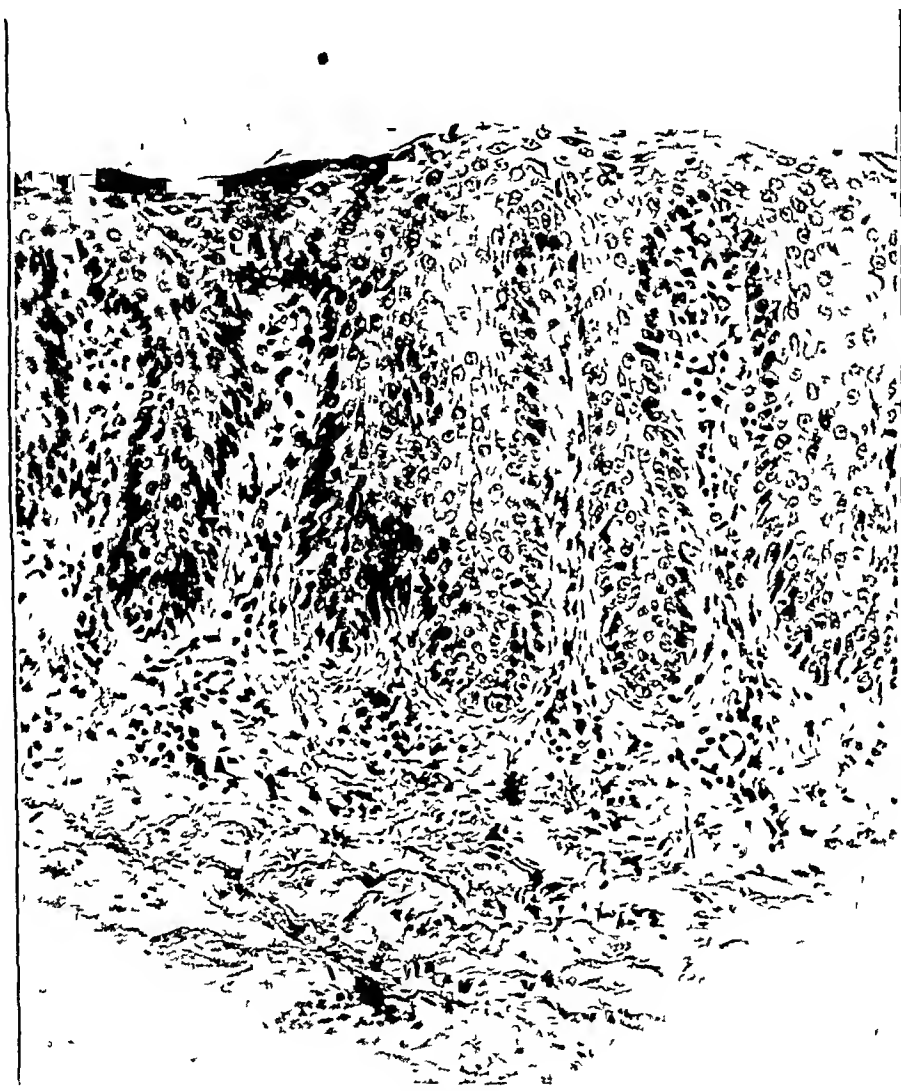


Fig 6 (case 3)—Epidermal cells show spongiosis, elongated rete pegs and perivascular infiltration of the dermis  $\times 90$

junction with the care of her family physician her eruption disappeared completely in four months. Six months have elapsed without recurrence.

#### COMMENT

These 3 patients presented several similar features, all were females, in each the eruption followed relatively soon after she had taken a sulfonamide drug, in each the appearance of the eruption warranted

a clinical diagnosis of psoriasis, and in 2 of the 3 the microscopic diagnosis was consistent with that of psoriasis, none of the 3 had a suggestive hereditary history, none had previous disturbances of the skin. The duration of the eruption in 1 was four months, and the skin has been clear six months. In another the lesions were present four months, cleared from the body but remained in the scalp for fifteen months and then reappeared and have been present ever since. The third still has lesions and has had them continuously for twenty-one months.

Speaking of the entire group, most of the essential features of psoriasis were encountered. The only ones constantly missing were changes in the nails. The interval between the patient's taking the drug and the beginning of signs relating to the skin was in most cases less than two weeks, the extremes being two days and four months. One elderly woman had had psoriasis as a girl and had been free from eruption for years, but after a course of sulfathiazole there was a prompt recurrence of her long dormant psoriasis. Another woman has had psoriasis of the lower parts of the legs each winter for five years following a severe infection of the throat, which was treated with large amounts of both sulfathiazole and sulfadiazine. In none of our cases were my colleagues and I able to persuade the patients to take sulfonamide compounds again except for the 8 year old girl with rheumatic fever. After withholding the drug for a number of months, her physician again prescribed it, and she is now taking 10 grains of sulfathiazole daily for one week out of each month.

#### SUMMARY

I have observed a series of cases of psoriasiform dermatoses, from which 3 cases are reported.

Study of these cases seems to indicate a sulfonamide drug as the cause.

Experience points to infective processes as an inciting factor in precipitating initial attacks of psoriasis, now apparently we may add another toxic agent—the sulfonamide compounds.

In speculation regarding these cases I think that there is suggested the possibility of the existence of psoriatic patients in whom the disease remains below the threshold of the eruptive phase until some potent excitant such as a sulfonamide drug precipitates an eruptive reaction.

No positive conclusions should be drawn from my few cases or from this limited research, but I hope that others, with larger facilities, may be stimulated to investigate this problem.

227 Sixteenth Street

#### ABSTRACT OF DISCUSSION

DR. BEDFORD SHELMIRE, Dallas, Texas. With the advent of the sulfonamide drugs, dermatologists began encountering cutaneous manifestations and allergic

phenomena somewhat different from those produced by the chemotherapeutic agents employed up to that time

In addition to the ordinary eruptions caused by drugs, rarer manifestations, such as pemphigus-foliaceus-like or varioliform eruptions, solar sensitivities, cyanoses, erythema nodosum, fixed eruptions, chronic discoid and acute disseminated lupus-erythematosus-like conditions and local and widespread eczematoid eruptions, have been repeatedly recorded as having been evoked by this group of chemical agents. In addition, the extracutaneous manifestations, such as drug fevers, swellings of joints, conjunctival hemorrhages and motor and sensory changes, are more frequently observed than in most sensitivities to drugs.

This group of drugs is almost unique in its ability to sensitize the skin to certain solar wavelengths. The sun-sensitizing index of the sulfonamide drugs seems especially high in Texas, where the solar exposure index is at a maximum. There are indications in certain instances either that the sulfonamide drugs are retained in the system for prolonged durations or at least that solar sensitivity persists for long periods after the ingestion or local application of the drug is completely withdrawn. I have observed 1 patient in whom there developed three separate attacks of acute solar dermatitis over the exposed areas two, four and six weeks after complete removal of the drug. In 2 other patients chronic discoid solar dermatitis of the cheeks and back of the neck, of six months' duration, followed the ingestion of sulfonamide drugs. Another patient, with chronic, recurrent papular-vesicular solar dermatitis of the face, ears and posterior surface of the neck, stated that his eruption followed the ingestion of sulfonamide drugs two years previously for the treatment of gonorrhea. I have seen several cases in which papular solar dermatitis of the exposed areas—face, arms and legs—persisted for six to eight months after removal of the sulfonamide preparation.

This group of drugs is outstanding in its ability to be absorbed through the skin after topical application. Widespread eruptions, especially of the eczematous type, are repeatedly seen after local applications even over small areas. When the drugs are applied to an area of preexisting dermatitis or open wounds, evidence of absorption and widespread dissemination may rarely be seen, even in the absence of evidence of local contact dermatitis. In my practice such severe focal flare-ups of existing sulfonamide eruptions or widespread incapacitating recurrences of healed eruptions followed patch tests with this group of drugs that the patch test has been completely abandoned and ingestion of  $\frac{1}{2}$  tablet has been substituted to prove cutaneous sensitivity to the sulfonamide preparation. Before abandoning routine patch tests with the sulfonamide compounds in cases of suspected sensitivity to these drugs, I provoked, in several instances, recurrences of healed eruptions which required six weeks or more to heal completely. Therefore patch testing with the sulfonamide drugs is not without danger. The eruptions evoked by this group of drugs, especially the eczematoid type, resemble those produced by iodides, bromides and arsenic because of the frequent prolonged time for healing after removal of the drug either by ingestion or by local application. Sulfonamide eruptions frequently require months to heal completely. I observed a generalized exfoliative dermatitis following the application of sulfonamide powder to a small cut on the finger require five months to disappear completely.

The sulfonamide drugs resemble phenylethylhydantoin in their ability to desensitize on continuous or frequently repeated ingestion, if the reports of the many English authors can be accepted.

Dr. Philpott has recorded an additional cutaneous variation to those previously recorded due to this group of chemotherapeutic agents. The photographs cer-

tainly depict psoriasiform eruptions, and the histopathologic changes in his cases are compatible with those of psoriasis. I have observed only 1 example of psoriasiform sulfathiazole dermatitis. The patient displayed widespread nummular lesions with mica-like psoriasiform scaling over the arms and legs. The eruption slowly disappeared after the cessation of ingestion of sulfathiazole, which had been almost continuous for two years.

DR. STUART C. WAY, San Francisco. My comments are based on the assumption that 2 of the 3 cases presented by Dr. Philpott represented cases of true psoriasis. First of all, it seems in order to state, regardless of the various theories already advanced, that the real causation of psoriasis is not known. Cutaneous eruptions due to drugs frequently imitate many of the common dermatoses. The data in the 3 cases presented by Dr. Philpott seem somewhat insufficient to establish the sulfonamide compounds as having actually produced psoriasis or an eruption closely resembling psoriasis. It is unfortunate that lack of cooperation on the part of 2 of his patients made it impossible to administer the sulfonamide drug longer. Dr. Shelmire's theory about desensitization may explain the failure of the dermatitis to recur in the third case. To complicate the etiologic problem further, the onset of the eruption was preceded in 2 of Dr. Philpott's cases by a so-called streptococcal infection of the throat and in the third by rheumatic fever. Of course, Dr. Philpott was mindful that infection is a possible cause of psoriasis, as many physicians have pointed out, and he goes ahead to mention in his paper that experience points to infective processes as a deciding factor in precipitating initial attacks of psoriasis. It should be borne in mind that psoriasis is one of the commonest diseases of the skin. Therefore it is logical to assume that according to the law of averages a certain percentage of new cases of psoriasis must develop during and after the administration of such widely used drugs as the sulfonamide compounds. I would like to suggest that the members watch for the sulfonamide drugs as a possible causative factor in new cases of psoriasis.

DR. ALFRED HOLLANDER, Springfield, Mass. I believe that all the members have seen cases of this type, and I think that the condition should be classified as true psoriasis. I made another observation which I believe belongs in this category. A salesman struck his leg against a counter, inflicting a slight abrasion. The physician who saw him applied sulfathiazole ointment for three consecutive days. The abrasion healed. A week later the man hurt his leg again on the same site. He went to the nurse, and again he was given sulfathiazole ointment to apply. Three days later, as he told me, he saw what he thought was a papular eruption in the injured region. I saw him a week later. He had a typical psoriasis plaque on the site of that injury, and still two weeks later he had typical psoriatic lesions distributed over the trunk and upper and lower extremities. Since this patient had never had psoriasis previously, the question arose whether or not the injury and the consequent application of the sulfonamide drug caused the psoriatic outbreak. He was seen by another dermatologist, who definitely declined to say that the eruption was a result of use of a sulfonamide drug. I believe that I told Dr. Louis Schwartz at the time about my observation. He had not seen anything of that kind.

I think that this case presents the most typical example of Koebner's phenomenon. All such cases can be explained accordingly.

## ATYPICAL LICHEN PLANUS TROPICALIS

MAJOR M G BUTLER

MEDICAL CORPS, ARMY OF THE UNITED STATES

**T**HE OBSERVATIONS and conclusions concerning the bizarre syndrome atypical lichen planus tropicalis are based on the study of this disease in a group of 247 cases. The patients were cared for at a debarkation hospital for evacuees by air from the Pacific Theater. Patients were seen during the period from October 1944 to September 1945.

In the first cases seen the condition was recognized as a new dermatologic entity, which showed some similarity to hypertrophic lichen planus. The violaceous papulosquamous lesions on the legs were clinically identical, and histologic sections were similar to a degree, although differing in the inflammatory reaction and intercellular edema. The large number of patients involved, the not infrequent deaths and the serious systemic involvement were entirely different. Polygonal shiny lesions characteristic of lichen planus did not occur.

The disease is manifested by an eruption in which the essential lesion is papulosquamous, initially occurring as pinhead-sized follicular papules. The earliest sites of involvement are varied, oftenest on the dorsum of the hands, the trunk or the upper part of the back. The initial lesions tend to coalesce, forming papulosquamous, violaceous, matchhead-sized to pea-sized lesions, which in turn coalesce until the entire skin or large areas are covered by thick plates of violet-gray desquamating skin. Secondary infection with pustules or oozing occurred in some 10 per cent of the cases. Fissures and ulcers were secondary in a few cases. The soles and the palms were often solid plaques, which cracked and bled on motion. Loss of hair in an alopecia-areata-like manner, frequently becoming total, was observed in the cases of severer forms. Grouped follicular papules occurred on scalps in which no hair was lost. The mucous membranes were involved in an eruption most frequently.

This material is original and was presented in a lecture May 8, 1945, at the Army Air Forces District Medical Conference. The original lecture has been amplified. Articles concerning the syndrome atypical lichen planus tropicalis have been published since this time, but they concern many less cases and the illustrations as presented have been less detailed. The serious eruptions considered here are entirely distinct from the larger group of eczematoid dermatitis with lichenification which involved the majority of men evacuated by air because of dermatologic diseases.

resembling leukoplakia associated with fissures and ulcers. Lesions resembling condyloma lata occurred on the genitalia and perianal tissues. Involvement of the mucous membrane was commonest on the lips, tongue and buccal mucosa and infrequent on the genital and anal mucosa. The nails were commonly involved, showing thickening and distortion, with loss of nails in a few instances. Generalized nonsuppurative, nonpainful lymphadenitis, with especially prominent enlargement of the inguinal lymph nodes, was demonstrable in the severe forms. Edema and venous stasis of the lower extremities were usual but perhaps a result of prolonged rest in bed. Systemic complaints of anorexia and severe intractable diarrhea associated with extreme weakness were common.

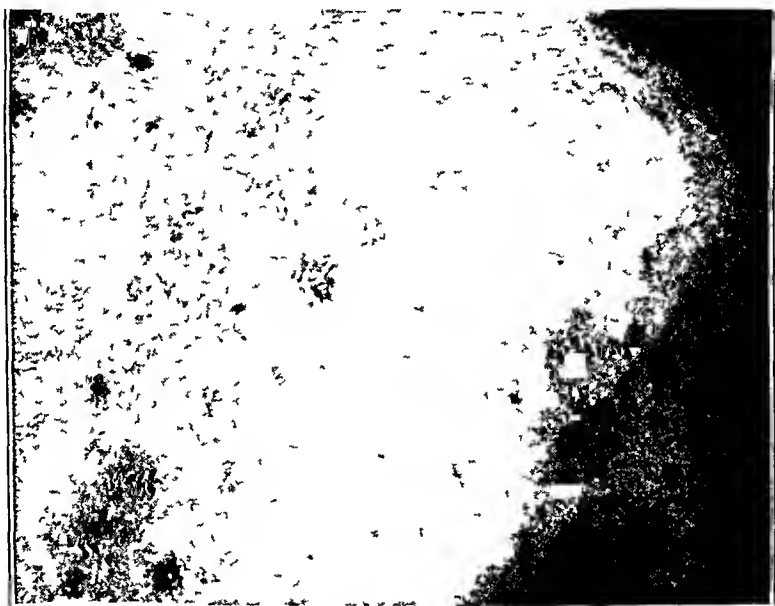


Fig 1—Early follicular lesions forming groups and coalescing to form the violaceous papules. Photograph of the shoulder, one of the common early sites of involvement. (Official photograph by United States Army Air Force.)

Cultures of the stools in such cases were negative for bacteria and amebas. The degree of pruritus varied from none to intolerable and did not correspond to the severity of the eruption. Complaints of sharp shooting pains in the legs and disturbances of vision were associated with neurologic findings of decrease in the visual fields and the presence of areas of anesthesia and paresthesia on the skin. Mental disturbances were usually a profound depression, with 3 patients having definite hallucinations and delusions.

The course of the disease seems to include a prodromal stage, in which recurrent pruritus of the skin is present without lesions, following a latent period, which varies from two weeks to two years. The usual



Fig 2—Hypertrophic lesions on the anterior surface of the legs, clinically identical with hypertrophic lichen planus (Official photograph by United States Army Air Force)



Fig 3—Patchy alopecia of the scalp This is the earliest form, and the alopecia later often became total (Official photograph by United States Army Air Force)

time of onset was approximately four months after a patient's arrival in the New Guinea area. Patients became progressively worse if not evacuated to the United States. Patients who had recovered in the United States or Australia relapsed when they returned to the New Guinea areas. Patients with a mild form of the disease seemed to recover spontaneously and within a few weeks, but severe forms continued without improvement for periods extending to five or six months. The development of lesions at sites of trauma was identical with that seen in true lichen planus. Striking residual brown pigmentation persisted for months after the cutaneous lesions subsided, and the regrowth of hair and return of nails to normal required an interval of months. Visual fields returned to normal rapidly, but the complaints of pains in the lower extremities were persistent even after decided improvement of the skin. The temperature remained within normal limits in most

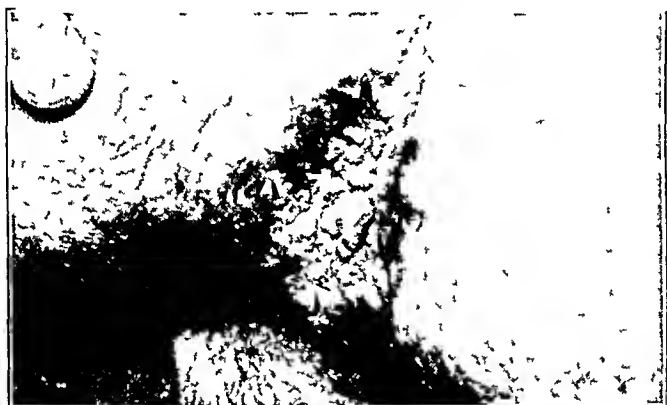


Fig 4—Papular lesions resembling condyloma lata as seen in syphilis (Kahn reaction negative) (Official photograph by United States Army Air Force)

cases. The hematologic findings were variable, but in a few cases the disease was associated with aplastic anemia. I saw 3 such patients but was unable to follow up their course after they left this hospital. A common finding was a relatively high eosinophilia, the count ranging from 2 to as much as 54 per cent. Two patients died while at this hospital, and several other deaths of victims of this disease occurred after their transfer to other hospitals. The 2 fatal cases are reported in detail with the postmortem study.

#### REPORT OF CASES

**CASE 1**—A white woman aged 27 had been overseas twenty-one months. Her initial lesions of the skin developed six months after her arrival in New Guinea. Dermatitis developed after an attack of dengue. She was hospitalized overseas for three months and had varied local treatment. Previous to the onset of her eruption she had taken 1 tablet of quinacrine hydrochloride (atabrine) daily for six months. At the time of evacuation to this country she had received no quina-

crine hydrochloride for a period of three months. Initial examination revealed an emaciated white woman having generalized exfoliative dermatitis with some edema and oozing of the skin. Violaceous papulosquamous lesions characteristic of atypical lichen planus were seen over the dorsa of the hands. She was profoundly depressed mentally and had been taking frequent and large doses of barbiturates. There were extreme weakness and anorexia with evidence of severe dehydration. She had not received medicaments or plasma intravenously, because no superficial veins could be entered through the thickened, edematous skin. Eight hours after arrival she became comatose and showed decided respiratory depression. The possibility that she had taken a large dose of barbiturates in an attempt at suicide was raised by the fact that a quantity of barbiturates was found in her luggage. Intrasternal administration of whole blood and respiratory stimulants of various types with dextrose in isotonic solution of sodium chloride were administered, but the patient died twelve hours later. The hemoglobin content was 102 per cent and the white blood cell count 17,400, with a differential count of 31 polymorphonuclears, 14 lymphocytes, 1 basophil and 54 eosinophils.

*Postmortem Observations*—*Skin* The skin showed generalized erythema, exfoliation and a dried exudate. Microscopic sections showed hyperkeratosis and parakeratosis, with acanthosis and an inflammatory infiltration of the corium in the papillary layer, in some areas there was a polymorphonuclear infiltrate of the epidermis, with intercellular edema and abscess spaces showing necrosis of the epidermis and collections of polymorphonuclear leukocytes, with an appreciable number of eosinophils. The pathologist reported the picture of exfoliative dermatitis combined with lichen planus.

*Spleen* The spleen contained numerous eosinophils and two small nodules similar to malpighian corpuscles but possessing, centrally, macrophages which showed epithelioid cells, fibrocytes and much acellular connective tissue. The lesions suggested healed tubercles of an unusual type.

*Gastrointestinal Tract* The gastrointestinal tract showed leukocytic infiltration of the submucosa and in some areas acute inflammation of the epithelial mucosa.

*Liver* Almost the entire tissue was abnormal. There were side by side evidences of atrophy and regeneration with multinucleated cells. Some large basophilic cells resembling megakaryocytes were present. Moderate proliferation of the bile ducts was present. The abnormal nodule grossly seemed to be adenoma of the liver but was associated with a peculiar cirrhosis. The pathologist stated, "We are not sure what the lesion is, and for descriptive purposes we label it 'adenomatous cirrhotic nodule of the liver'."

*Brain* Pericellular and perivascular spaces containing fibrin shreds were associated with cerebral edema and associated vascular damage, with some leukocytic infiltration of the perivascular tissues.

*Pathologic Diagnosis*—The diagnosis was dermatitis, exfoliative and lichenoid, gastritis, acute, focal and slight, ulceration of the gastric mucosa, and colitis, acute, focal and slight. The brain showed edema and pericellular and perivascular inflammation of the cerebrum and cerebellum. No evidence of barbiturate poisoning was found.

CASE 2—A white man aged 39 had been overseas twenty-seven months. His initial lesions of the skin developed four months after his arrival in New Guinea. He had taken 1 tablet of quinacrine hydrochloride daily for a period of ten months. He was hospitalized overseas for six months. On arrival at this hospital his previous exfoliative dermatitis had subsided, showing only residual dryness and

pigmentation There were profound mental depression, loss of memory, mental confusion, partial loss of vision, severe anorexia and intractable diarrhea The mucous membranes of the tongue and mouth were reddened and dry and showed some ulcers of a superficial type There was definite tenderness of these membranes The patient had lost 37 pounds (168 Kg) Blood cell counts revealed secondary anemia The patient was treated by transfusions of whole blood, injections of liver intramuscularly, multivitamins, intravenous administration of dextrose and large doses of penicillin intramuscularly He remained weak despite the transfusions and became increasingly confused mentally, and four days before death a dry cough developed Physical examination revealed a few mild rales at the bases and some dulness to percussion Death occurred six weeks after admission During this interval he had received a total of twelve transfusions and 3,600,000 units of penicillin, without even temporary improvement Clinically, the diagnosis was atypical lichen planus tropicalis complicated by generalized exfoliative dermatitis and pellagra plus terminal pneumonia

*Postmortem Observations*—The patient was grossly an emaciated white, middle-aged man showing generalized pigmented scaling areas of skin over the entire cutaneous surface

*Skin* Atrophy was present, with loss of rete pegs The basal layer was partially destroyed, and the epidermal cells showed edema and degeneration The upper layer of the corium showed a bandlike, chronic, inflammatory infiltrate consisting of lymphocytes and mononuclear cells with a rare polymorphonuclear leukocyte Some deposits of melanin were noted The collagen showed degenerative changes The picture was consistent with that of healing lichenoid dermatitis Sections from another area of skin showed parakeratosis and acanthosis, with numerous broad rete pegs and some clubbing The basal layer was partially destroyed, and the papillae showed vascular dilatation and edema, with formation of new capillaries There was a chronic, inflammatory infiltration around the appendages of the skin and blood vessels The sweat glands showed slight degenerative changes The picture resembled a psoriasiform lesion (These descriptions are those of a general pathologist It was impossible to obtain slides for personal examination)

*Brain* The brain was slightly enlarged, weighing 1,600 Gm The vessels over the cerebral convolutions showed generalized congestion There was a diffuse increase of glial cells in the cerebral cortex, including astrocytes and macroglial and microglial cells Occasional ganglion cells showed degenerative changes, with vacuolation of their cytoplasm There were areas of perivascular polymorphonuclear and lymphocytic infiltration In the cerebellum a similar infiltration had occurred around the blood vessels Sections through the third ventricle revealed accumulations of large numbers of myelin bodies in the brain substance Sections through the thalamus and mamillary bodies revealed some degeneration of ganglion cells and two focal areas of hemorrhage Several minute foci of hemorrhage were noted in the basal ganglions and brain stem

*Peripheral Nerves* A loss of nerve fibers and myelin sheaths was noted in the peripheral nerves included on sections of skeletal muscle

*Heart* There were focal areas of degeneration, with vacuolation of myocardial fibers, fragmentation and even total loss of individual fibers Scattered inflammatory cells were noted throughout the myocardium, consisting of lymphocytes, mononuclear and polymorphonuclear leukocytes

*Lungs* Extreme congestion and scattered focal areas of hemorrhage were present There was patchy profuse infiltration by leukocytes Numerous macro-

phages were seen around blood vessels and beneath areas of slightly thickened pleura

**Lymph Nodes** The lymphatic sinusoids were packed with polymorphonuclear leukocytes and scattered red blood cells. Numerous macrophages filled with granular black pigment were seen in the medulla of the lymph node. Sections of several other lymph nodes revealed no follicular hyperplasia but, rather, a generalized increase in lymphocytes, with edema and congestion.

**Gastrointestinal Tract** The mucosa throughout showed mild evidence of inflammatory reaction, and the sections revealed an infiltration similar to that seen in the corium of the skin. Again, numerous macrophages containing black pigment were noted.

**Liver** There was a generalized increase in hepatic fibrous tissue and numerous hepatic cells having two nuclei. Some hepatic cells contained clear vacuoles.

**Pathologic Diagnosis**—The pathologic diagnosis included degeneration, focal and acute, of the myocardium, severe bronchopneumonia, acute and organizing, in all lobes of both lungs, congestion and edema of the lymph nodes, passive and chronic congestion of the liver, sporadic degeneration of the ganglion cells, cerebrum, thalamus and brain stem, hemorrhages and petechiae, thalamus and brain stem, degeneration of the ganglion cells, anterior horns and cervical cord, degeneration of the peripheral nerve fibers, chronic lichenoid dermatitis, which was healing, and mild exfoliative dermatitis.

**Comment by Pathologist**—This soldier apparently suffered from a chronic, lichenoid type of dermatitis which was progressive and developed into exfoliative dermatitis. Despite minimal pathologic changes in the gastrointestinal tract, he suffered from diarrhea, and subsequently degenerative changes developed in the central nervous system and peripheral nerves. The bronchopneumonia subsequent to debility is sufficient to account for death.

#### COMMENT

As to the cause, this is the type of dermatitis seen in patients returning from the Pacific theaters with a history of therapy with quinacrine hydrochloride. The cause of the changes in the nervous system is obscure but may be a result of vitamin deficiencies resulting from the diarrhea. The changes seen in the heart and various organs may be due to multiple deficiencies of the vitamin B complex group or to toxic factors as a result of either the exfoliative dermatitis or the same agent which caused the dermatitis.

Clinically, this new entity occurred in men and women, with an apparent increased susceptibility of women. One out of every 12 patients was a woman, a much greater proportion than the relative number of women in the Pacific area. There were persons of all ages, from 17 to 60, with, of course, the greater number in the age group common to the Army, i. e., 20 to 30. No race possessed immunity. Patients seen by my associates and me included Negroes, Indians, Chinese, Filipinos and white persons, in proportion to the numbers in the area. A careful study of the past and family histories failed to reveal any significant incidence of previous cutaneous disease, allergies or susceptibility to pyogenic infections. The disease occurred impartially in emotionally unstable and phlegmatic patients. The officers were as frequently involved as

enlisted men. Several common factors concerned all these patients. First, they were all taking quinacrine hydrochloride in doses of 1 or more tablets daily. Second, they were all stationed in the area of or near the latitude of New Guinea. In some persons the eruption developed after they had left these areas, occasionally even during the first few days after arrival in the United States. Most of the patients had been actually ashore in New Guinea, Morotai, Biak or Burma, but some 12 patients were never ashore but did live on shipboard near these land masses. This territory has a climate which is hot, with the temperature in the day frequently 90 to 130 F and a humidity of nearly 100 per cent. The men were malnourished, with an average loss of 20 to 40 pounds (9 to 18 Kg). This was a result of the climate and the lack of palatability of dehydrated foods. After a few weeks of eating these foods men often subsisted on coffee and doughnuts, refusing the other foods. Fresh vegetables, milk and meats were practically never seen. A few cases occurred, however, among medical officers who took vitamins regularly and forced themselves to eat a balanced diet. The incidence of true lichen planus among evacuees by air was no more than the incidence of this disease among a similar group of civilians, and in the cases of true lichen planus the conditions were not serious. Consideration of quinacrine hydrochloride as a cause of this syndrome was prompted by the use of quinacrine hydrochloride by all troops. Against this being the true cause, in my opinion, is the fact that experimental doses of quinacrine hydrochloride in larger doses in a group of volunteer students did not produce atypical lichen planus tropicalis. Doses were continued for several weeks but, of course, not for the prolonged periods in which quinacrine hydrochloride was taken overseas, nor was the number participating large enough to rule out the possibility of an idiosyncrasy evident in the larger groups of troops. Atypical lichen planus tropicalis was not reported in the other theaters where quinacrine hydrochloride was used. A nationally known dermatologist with experience in the African and Italian theaters examined patients with me and declared that the syndrome was entirely different from any seen in those theaters. Intelligent patients, including physicians and dentists, maintained that while they had taken quinacrine hydrochloride for from one to two years in other areas atypical lichen planus tropicalis did not develop until some time after their residence in the New Guinea area. In Filipinos who had lived on Luzon all their lives and who had taken quinacrine hydrochloride while stationed in the Philippines, the disease developed after transfer to New Guinea. These patients maintained that both natives and Japanese in the New Guinea area had a similar eruption. Reactions to passive transfer tests and patch tests to quinacrine hydrochloride were negative in 6 cases checked. Finally, the continued use of quinacrine hydrochloride did not prevent or retard

recovery of a test group compared with a group under identical treatment who received no quinacrine hydrochloride during treatment. Three patients from whom quinacrine hydrochloride had been withdrawn for more than six months showed no improvement until treated with penicillin.

Treatment of these patients was largely symptomatic and empiric. Baths in starch and sodium bicarbonate were used twice daily for cleaning and relief from pruritus. In uncomplicated forms 2 per cent salicylic acid in cold cream was applied after the baths. The patients received a special high vitamin, high caloric diet. They were given multivitamins and, in some cases, liver extract intramuscularly. After treatment of 1 patient with a complicating pyoderma by the use of intramuscular injections of penicillin, his atypical lichen planus of more than six months' duration cleared within three weeks, and he was discharged to duty, with only residual pigmentary changes. This patient had no relapses during the subsequent six months. After this result all patients with severe eruptions were treated with 320,000 units of penicillin daily for a period of eight days. Approximately 80 per cent showed an immediate improvement, with gains in strength and weight accompanied with flattening of their cutaneous lesions. These patients were transferred to a special hospital within ten to twenty days, and I had no opportunity to follow their further progress. Application of penicillin locally where only a few lesions were present similarly produced involution of the lesions within a period of seven to ten days and reduced pruritus.

#### CONCLUSIONS

The clinical picture of a severe, systemic disease associated with a papulosquamous violaceous eruption resembling hypertrophic lichen planus is described.

The theory that quinacrine hydrochloride is the cause of this eruption is discussed but does not appeal to me as the true cause, although it may have been a contributing factor in producing porphyrin bodies which sensitized the skin.

The probability that a systemic infection by some unknown infectious agent having geographic limitations to the New Guinea and surrounding territories is a better explanation of the picture presented. The possibility that the infectious agent is transmitted through an intermediate host, such as an insect, has been inadequately explored. Another possibility is that the eruption is an unusual idlike response to infection of the skin by staphylococci, a common and serious cutaneous infection in the tropics, to date, however, no recurrence of atypical lichen planus tropicalis has been observed, while such recurrences have been common in patients with the more frequent infectious eczematoid dermatitis returning from the tropics.

It is felt that the term atypical lichen planus tropicalis is a poor one for the syndrome and should be used only until final determination of the true causation

502 South Jefferson Street, Saginaw, Mich

#### ADDENDUM

Since the presentation of this article a summation of opinions concerning the described disease has been published in the *Bulletin of the United States Army Medical Department*. Evidence of occurrence in other geographic areas increases the probability of quinacrine hydrochloride being considered an etiologic agent

## Obituaries

### ERICH URBACH, M D

1893-1946

Erich Urbach died of coronary thrombosis in Philadelphia Dec 17, 1946, at the comparatively early age of 53. He is survived by his wife, Dr Josepha Urbach, to whom he was married July 29, 1921, and by two sons, Fred, an intern in the Jefferson Medical College Hospital, and John, a senior medical student at the University of Pennsylvania School of Medicine.

Urbach's education evidences the continental thoroughness of preparation for a life work. Thirteen years in the schools and Imperial Staats-Gymnasium of his birthplace, Prague, Czechoslovakia, was followed by two years (1912 to 1914) of study in the School of Medicine of the University of Vienna, interrupted by World War I and resumed in 1918. During the first world war he served as lieutenant in the Austrian army, attached to the surgical service of Eiselberg, twice received the Gold Cross of Merit for valor and was awarded a silver Medal of Honor from the Red Cross. From 1918 to 1920 he interned in the Allgemeine Krankenhaus, Vienna, Austria, in 1920-1921 was on the staff of the elder Jadassohn at Breslau, Germany, and from 1921 to 1923 was resident in internal medicine at the Allgemeine Krankenhaus. From 1923 to 1928 he served under Koenigstein at the Jewish Hospital, Vienna, Austria, and in 1923 was made a Fellow of the Vienna Board of Dermatology. In 1928 he became assistant chief under Kerl in the Department of Dermatology and Syphilology of the University of Vienna and in 1929 became associate professor. From 1936 to 1938 he headed the Department of Dermatology and Allergy of the Merchants' Hospital.

In April 1938 Urbach came to the United States as a war *émigré*, from that date to the time of his death he was associate in dermatology at the University of Pennsylvania School of Medicine, practiced in Philadelphia and, since 1929, headed the Allergy Department of the Jewish Hospital. His society memberships included the Vienna, Hungarian, Polish and Turkish dermatological societies and the College of Physicians of Vienna. He was a member of the Philadelphia Society of Allergy and a regent of the American College of Allergists.

An examination of Urbach's publications, numbering two hundred and eleven papers and five books plus a second edition of his "Allergy," shows him to have been one of the most productive workers of his day.

and field. An analysis of the papers by title and journal of publication discloses further his remarkable range. Twenty-seven papers deal with pathology, thirty-one with physiologic chemistry, ten with endocrinology and metabolism, two with internal medicine and forty-five with clinical dermatology. Allergy, the field of his major effort, is represented by ninety-seven papers. Their chronology and the standing of the journals publishing his communications show the validity of his basic scientific training in pathology and physiologic chemistry, acquired under Paltauf and Fuerth in the Institute of Experimental Pathology. He was, moreover, an omnivorous reader and an indefatigably alert student and observer, which gave him an acquaintance with literature and an ingenuity in method that was the envy of associates and the admiration of students. He moved at high intellectual speed, and it is not surprising that some of his conceptions and assertions are still unappreciated or unchecked. His contributions to the lipoidoses of the skin alone would have justified him as a dermatologist.

To evaluate Urbach fully as an investigator is obviously at the present time impossible, since it will involve extensive confirmatory and critical laboratory work that few are fitted to undertake. It may be said without hesitation that his experimental work is alive and challenging and at the forefront of his day and deserves prompt recheck because of its basic importance in the comprehension of mechanisms of cutaneous reaction. He brought to one American clinic, at least, a new and stimulating outlook on carbohydrate metabolism, on photosensitivity and on the import and domain of allergy in dermatology. From one angle or another he was constantly shedding new light on clinical problems, the bacterial flora of the intestine one moment, dietotherapy the next and the pathologic changes of periarteritis nodosa the next. He appreciated the psychogenetic, as one would hardly expect from his tradition, and once in his Vienna clinic he pointed out to me, in a humorous moment, the psychotherapeutic importance of the large glass insert in a conduit evacuating colonic irrigation fluid, placed so the patient could observe it.

As a teacher Urbach was greatly appreciated, for he possessed analytic power, grasp, incisiveness, knowledge of medicine at large and of the literature and convictions. Even before his command of English became adequate, listening to him was a pleasure because of the faceted quality of his thought, and he was in special demand among interns to discuss a referred case. Graduate students who sat under him in Vienna have expressed warmly their appreciation of his teaching. One of his finest qualities was his willingness to lay all his cards on the table in diagnostic analysis and treatment. One could forgive him occasional prejudice, for one knew that he never withheld any part of his intellectual resource. His associates constantly drew on him

for his encyclopedic acquaintance with the literature and his intimate knowledge of continental methods of treatment, based on masses of material and experience rare in this country. His occasional excursions into nomenclature, which have irritated even some of his otherwise admiring critics in allergy, were side expressions of a continental analytic tradition inevitable at the Hebra center of the dermatologic universe.

As faculty associates, his passing leaves us all with a deep sense of loss. To us he was *Kollege* in the fullest sense. He shared, and he never shirked. He worked himself ruthlessly, contributed cases and disputation, made rounds, thought, wrote and spoke vividly, challenged one's critical faculties and upset one's complacencies and torpors. His advent was a genuinely refreshing experience. At an age when change is not too well received in a professional life, he had changed environment, language, associates and economic and professional status and weathered it all with benefit of many warm friends and despite a few good enemies. His record and achievements speak for themselves and would have graced a much longer life.

JOHN H. STOKES, M.D.

## Correspondence

### ANGIOMAS OF THE SCROTUM

*To the Editor* —Regarding angiomas of the scrotum (angiokeratoma, Fordyce), Robinson and Tasker (ARCH DERMAT & SYPH 54 667-674 [Dec ] 1946) concluded that their "reported case is the first in which angiomas of the tongue were associated with those of the scrotum" I call attention to a statement I (Sutton, R L, and Sutton, R L, Jr Diseases of the Skin, ed 10, St Louis, C V Mosby Company, 1939, p 668) published in 1939, that "in all such cases seen by the junior author, the tongue showed beneath it and along its border the telangiectases which characterize Osler's disease, one manifestation of which vascular anomaly we believe scrotal angiokeratoma to be" That sentence ought by now to be revised to read, "In several such cases"

I hesitantly claim priority for my observation, which—if Robinson and Tasker saw it—was not, they could correctly rebut, a formal report of a case Sutton Sr and I have often remarked what sharp eyes were possessed by many men, some of them long dead

If this addendum to Robinson and Tasker's article contains any generality, it is that a claim for priority can be justified if and only if a most careful and tedious search of records (hardly worth the while) has proved fruitless Clinically, things are seldom seen which have not been seen before, although interpretations vary almost from day to day

RICHARD L SUTTON JR, Kansas City, Mo

## News and Comment

### GENERAL NEWS

At a recent meeting of the American Board of Dermatology and Syphilology, it was voted to abolish group A as of Jan 1, 1949 On and after that date all candidates for the certificate of the board must submit proof of three full years of training in an approved institution

## Abstracts from Current Literature

CONGENITAL GLAUCOMA FOLLOWING MATERNAL RUBELLA DU PONT GUERRY III,  
Am J Ophth 29 190 (Feb) 1946

Two cases are reported of congenital glaucoma following maternal rubella during the first and second months of pregnancy

OCULAR LEPROSY IN PANAMA R D HARLEY, Am J Ophth 29 295 (March) 1946

The effect of leprosy on the eye has been studied in 150 cases in Panama. Seventy per cent of the patients were natives of Panama, the remainder came predominantly from the bounding countries and the West Indies. Ninety per cent of the patients of a leprosarium were found to have ocular involvement. Impaired vision is common in leprosy. Thirteen per cent were totally blind, and an additional 41 per cent had vision reduced to 20/200 or less. The anterior segment of the eye is by far more frequently involved than is the posterior segment. Superficial punctate keratitis or pinpoint lepromas of the irises are so typical as to be diagnostic of ocular leprosy. Glaucoma is not common. Absolute corneal anesthesia is rare, but relative loss of corneal sensitivity does occur.

Prophylaxis for leprosy eyes through protection with dark glasses or goggles is indicated. The factor of protection has been underemphasized in the past.

Therapy is largely confined to palliative measures. Solution of thyroxin used topically may be of aid in helping to clear corneal infiltrates. The leper withstands surgical treatment of the eye better than one might suspect. Operation on the lids produces gratifying results.

THE LICHEN PLANUS-ECZEMATOID DERMATITIS COMPLEX OF THE SOUTHWEST PACIFIC ERVIN EPSTEIN, Bull U S Army M Dept 4 687 (Dec) 1945

The author reported a study of 65 cases. The disease is the most frequent cause of evacuation for cutaneous diseases from the Southwest Pacific area. The dermatitis is usually of the hypertrophic type. The lesions are purplish coalescent nodules. The mucous membranes of the mouth are often involved, but some extensive conditions do not present such involvement. The lesions look like lichen planus but present many unusual features, including atypical localization, occasional atrophic sequelae, abnormal histologic features, lack of typical lichen planus papules and unusual hyperpigmentation. In addition, the frequent transformation into an eczematoid, exfoliative, dermatitis-like eruption is at best an extremely unusual manifestation of lichen planus, while it is not uncommon in the syndrome described. The complications described are pyogenic, residual or recurrent dermatitis, pigmentary changes, disturbances in the sweat mechanism and psychogenic complications. The most important laboratory finding is hypoproteinemia.

Among the causative factors are (1) quinacrine hydrochloride (atabrine), (2) contact dermatitis and (3) mycoses. The treatment is nonspecific and not too efficacious, consisting in soothing applications of wet packs. Sulfonamide drugs and penicillin have no effect. The eruption starts to improve, as a rule, as soon as the patient leaves the Southwest Pacific, although many months are usually required for complete clearing.

REACTIONS TO PENICILLIN FRANK E CORMIA, LEIF Y JACOBSEN and E L SMITH, Bull U S Army M Dept 4 694 (Dec) 1945

The study deals with the serious and unusual reactions obtained in some 2,000 soldiers receiving prolonged courses of penicillin. Serious reactions have been

reported in about 0.5 per cent of the patients reported. Reactions may occur shortly after initial exposure to penicillin, as a result of an existing hypersensitiveness, or at later intervals, because of developing sensitization. Both early and late reactions may be serious in nature and require discontinuation of therapy. From clinical observations, it appears that the primary shock tissue in most reactions to penicillin is the vascular bed.

Intradermal testing with penicillin has been of limited value as an aid in diagnosis and a guide for further treatment. Increased reactivity to penicillin may occur on the basis of a previous acute fungous disease.

**SKIN SENSITIVITY DUE TO ATABRINE** RICHARD WHITEHALL, Bull U S Army M Dept 4 724 (Dec) 1945

The author reported an eczematous dermatitis involving the eyelids and the areas behind the right ear due to quinacrine hydrochloride (atabrine). A positive reaction to a patch test with quinacrine hydrochloride was obtained.

**DERMATITIS FROM ATABRINE** L. M. NELSON, Bull U S Army M Dept 4 725 (Dec) 1945

The author reported a case of pruritic dermatitis of the wrist which finally spread to involve the whole body and a second case of a generalized dermatitis which eventually developed into a generalized exfoliation. Positive reactions obtained by patch testing with powdered quinacrine hydrochloride (atabrine) were interpreted to be a manifestation of hypersensitivity rather than of a primary irritant, since 8 patients with other dermatoses tested in the same manner did not react similarly.

STRAKOSCH, Denver

**THE ANTIBACTERIAL AND FUNGISTATIC PROPERTIES OF PROPAMIDINE** WILLIAM O ELSON, J Infect Dis 76 193 (May-June) 1945

Propamidine (4,4'-diamidinodiphenoxypropane) was first synthesized by Ewins and his co-workers in the course of their studies on the trypanocidal activity of aromatic diamidine compounds and was shown to possess well marked activity against various protozoal organisms. Subsequently, Thrower and Valentine demonstrated that this compound had considerable antibacterial action against gram-positive cocci, both in vitro and clinically in the treatment of infected wounds and burns. These findings were verified in reports from several other clinical investigators.

Despite extensive investigations, there have been no reports in the literature of studies concerned either with the general antibacterial spectrum of this agent or with its fungistatic activity against the common pathogenic fungi. In the course of investigations carried out in Elson's laboratory, these properties have been studied and serve as the basis for this report. In this, the author presents the antibacterial spectrum of propamidine against representative gram-positive and gram-negative organisms. He studied the fungistatic action of propamidine as related to a number of the common superficial and deep pathogens. The sensitivity of some of these organisms compares with that of the gram-positive cocci. The antagonistic effects of a phospholipid on the fungistatic action of propamidine can be demonstrated. There is an important relation of hydrogen ion concentration to bactericidal activity of propamidine from the standpoint of competitive cationic adsorption.

**ROCKY MOUNTAIN SPOTTED FEVER** CHARLES C SHEPARD and NORMAN H TOPPING, J Infect Dis 78 63 (Jan-Feb) 1946

The authors performed complement fixation tests with Rocky Mountain spotted fever antigen on serums of dogs from several parts of the country. They obtained high-titered reactions in serums from known areas of spotted fever. The incidence of strongly positive reactions was greater in the dogs selected for their proximity to human patients with the disease.

CORNBLEET, Chicago

PENICILLIN LEVELS IN SERUM AND SOME BODY FLUIDS DURING SYSTEMIC AND LOCAL THERAPY EDWIN M ORY, MANSON MEADS, BRUCE BROWN, CLAIRE WILCOX and MAXWELL FINLAND, J Lab & Clin Med 30 809 (Oct) 1945

The authors report their observations on penicillin levels in serum and in some of the body fluids which are commonly infected with susceptible organisms. The data were obtained almost entirely on patients while under treatment with various doses of penicillin given by different routes.

The penicillin was usually given in 0.85 per cent solution of sodium chloride, except in patients with cardiac disease, in whom the continuous injections were given in 5 per cent dextrose solution, and in those treated by inhalation. The concentration of penicillin in the body fluids was determined by the serial dilution method of Rammelkamp. A strain of hemolytic streptococcus no 98, obtained from Dr C S Keefer, was used throughout. Human group O cells were used as an indicator in tests with body fluids in order to avoid the nonspecific hemolysis observed when horse cells are used.

Their results were as follows. During continuous intravenous and intramuscular infusion, fairly constant levels were maintained in the serum of any given patient, but the levels may vary in different patients on the same dose. They found that continuous intravenous infusions when given for more than forty-eight hours may give rise to thrombophlebitis, and the continuous intramuscular infusions were more difficult to regulate and often painful.

During intermittent intramuscular injections a range of serum levels, but not exact values, can be predicted for the interval between doses in any given schedule of dosage. Larger doses resulted in serum levels which were sustained longer and at higher values than smaller ones. They were not able to find any detectable penicillin in the cerebrospinal fluid when given via the intermittent intramuscular route. The levels in pleural, peritoneal and synovial fluids were erratic and usually lower than levels in the serum.

The diffusion of injections of penicillin into the body cavities out into the serum was erratic, but adequate concentration usually remained in cerebrospinal, pleural and pericardial fluids for twenty-four hours and sometimes forty-eight hours or longer after local injections of large amounts.

After inhalations of penicillin from nebulized solutions, small amounts of penicillin may be detected in serum for short periods but rarely longer than two hours.

ATTEMPTED TRANSMISSION OF HUMAN LEUKEMIA IN MAN J B THIERSCH, J Lab & Clin Med 30 866 (Oct) 1945

Since it is known that in mice, guinea pigs and fowls leukemia can readily be transmitted, with a minimal amount of cellular material, in inbred strains, the author attempted transmission of human leukemia in a large number of patients with carcinoma and other chronic diseases with a life prospect of less than two years.

The materials used were cellular suspension of lymph nodes or suspension of splenic material (removed at autopsy) or blood from living leukemic patients. It was always fresh and injected between twenty minutes and one hour after it had been taken from the patient. All materials used were bacteriologically sterile. The bloods of the recipients were examined before inoculation of the leukemic material, daily for a week and then weekly for three months, following which they were observed monthly. Whenever possible, postmortem examinations were conducted on all patients inoculated.

The authors also attempted cross transmission of chronic myeloid leukemia to patients with chronic lymphatic leukemia and vice versa, in order to see whether patients with one type of leukemia were susceptible to the other type.

All transmission attempts from one person to another and cross transfusion between patients with leukemia failed within a two year period of observation. The author feels that the negative results obtained do not mean that leukemia is not transmissible but were mainly due to unsuitable recipients and unsuitable routes of transmission.

GELBER, Los Angeles

SCLERODERMA WITH INVOLVEMENT OF THE VISCERA REPORT OF CASE D G PUGH, W F KVALE and HAROLD MARGULIES, Proc Staff Meet, Mayo Clin 20 410 (Oct 31) 1945

A case of scleroderma is reported in which roentgenologic examination revealed changes in the esophagus and small intestine due to scleroderma. There also was scleroderma of the lungs in this case. Some involvement of the colon and heart by scleroderma was suspected but could not be determined with certainty. Characteristic sclerodermatous changes of the skin were present. The lesions of scleroderma result from an abnormal change in the collagen and terminate in induration of the tissue. Connective tissue in almost any part of the body may be affected by scleroderma.

FRUMESS, Denver

SELF-DISINFECTION OF THE SKIN A SHORT REVIEW AND SOME ORIGINAL OBSERVATIONS J M L BURTENSHAW, Brit M Bull 3 161, 1945

Burtenshaw reviews the literature on self disinfection of the skin and concludes that the disinfectant power rises with increased acidity. The authors who found that acid sweat is a good culture medium may have used an unreliable method of recovering bacteria from the skin, namely, swabbing. Further, the long chain fatty acids are not present in sweat, they are mainly secreted in the sebum and cling to the surface of the skin, where they may be sufficiently concentrated to kill even the staphylococcus. Ether extract from hair was analyzed and the different fractions examined for streptococcicidal power. Only fractions containing fatty acids and soaps were active. The inactive fractions were esters of fatty acids, sterols and higher alcohols. A number of fatty acids were tested for streptococcicidal power. Those with longer chains, capric, lauric, oleic and stearic acids, and, less actively, their soaps killed the streptococcus. The unsaturated oleic acid was more active than its saturated homologue, stearic acid. The more acid the solution used, the better its bactericidal power, but certain substances found in the skin and its secretions and lactic, citric and ascorbic acids were inactive against *Streptococcus pyogenes*. The whole range of acids of the acetic series, from formic to stearic and oleic, and, to a lesser degree, their soaps are important agents in killing bacteria, fungi and viruses on the surface of the skin.

THE SKIN AND THE RETICULAR TISSUE A H T ROBB-SMITH, Brit M Bull 3 172 1945

The term reticulosis is a generic morphologic title to describe a group of changes characterized by progressive hyperplasia of the cells of the reticular tissue, and it is usually restricted to the conditions in which the cause of the hyperplasia is unknown, however, in a broad sense, reticulosis could include the cellular reactions in typhoid or tuberculosis. The chief sites of the reticular tissue are the blood-forming organs, but connective tissue is also a part of reticular tissue, the dermis is but a specialized form of connective tissue, and it is in the dermis that reticular proliferations are observed. Of the leukemias, cutaneous lesions are most commonly observed in lymphatic leukemia and may consist of diffuse erythroderma or nodular purplish tumors affecting the face or small nodules scattered on the body. Sometimes the nodules may be limited to the conjunctivas or eyelids. In Hodgkin's disease, true involvement of the skin by lymphadenomatous tissue is rare and usually takes the form of plaques on the trunk with a tendency to ulceration. Lymphoid follicular reticulosis (follicular lymphoblastoma) is not uncommon. It is a relatively benign disease, with a survival period of ten or more years, which occurs between the ages of 40 and 50, usually presenting generalized enlargement of the lymph nodes and sometimes associated with hepatosplenomegaly. The cutaneous lesions, when present, take the form of multiple small nodules on the face or trunk, which may regress spontaneously, leaving soft depressed scars. The histologic picture is characteristic. There are large follicles of lymphoblast cells lying in a stroma of small lymphocytes. Mycosis fungoides differs from

many reticuloses in that the cellular proliferation of the tumorous lesions occurs in the superficial dermis and spreads intraepithelially. A striking feature of mycosis fungoides is the long prodromal stage, and in this stage the histologic changes are not characteristic. The lipidoses are a group of diseases in which there is a progressive hyperplasia of the reticular cells associated with an excess of lipid within the cells themselves. In the lipidoses it is not known whether there is a generalized disturbance of lipid metabolism, with the abnormal lipids taken up by the reticular cells, or whether there is merely a disturbance of intercell metabolism of the reticular cells with retention of lipid within the cytoplasm. Lipomelanotic reticulosis (exfoliative erythroderma with lymphadenopathy) is a group characterized by generalized exfoliative dermatitis in men of the fifth to seventh decades invariably pruritic, in which the color of the skin ranges from *homme rouge* to a dark brown. There is generalized lymphadenopathy, sometimes hepatosplenomegaly, and the hemogram shows neutrophilic leukocytosis with eosinophilia, sometimes of extreme degree. Lymphocytoma cutis, the Spiegler-Fendt sarcoid and histiocytoma have been classified as benign reticular tumors of the skin, whereas Kaposi's angiosarcoma is considered a malignant reticular tumor with certain similarities to mycosis fungoides—a slowly progressing prodromal stage with a later, rapidly progressing malignant stage. The theories of the pathogenesis of reticular hyperplasias are not discussed, nor is there any attempt to link these with the diseases of the ground substance of connective tissue, such as dermatomyositis or disseminated lupus erythematosus.

SCIENTIFIC PRINCIPLES IN THE DESIGN AND CHOICE OF OINTMENT BASES H BERRY, Brit M Bull 3 182, 1945

When oils or fats are absorbed by the skin, the main route is via the hair follicles and through the sebaceous glands. The intact epidermis itself is not penetrated to any appreciable extent. In general, the skin is impervious to most aqueous preparations, although certain medicaments have the faculty of penetration and absorption irrespective of the medium in which they occur, mercury and the mercurials methyl salicylate, salicylic acid and boric acid are capable of passing through living intact skin.

The condition of the skin may be the determining factor in deciding on an ointment base. On an excessively dry skin an oil in water emulsion may be used, while in seborrhea a water in oil emulsion might be preferable, while petrolatum should be avoided. A purely oleaginous base such as petrolatum has been criticized in that (a) its greasiness interferes with radiation of heat from the skin, (b) it does not mix with or absorb serous discharge and (c) it is disliked by the patient because of its greasy and clothes-soiling character. Of the bases producing water in oil emulsions, wool fat and wool alcohols are the most important. Wool alcohol is a brown wax, representing a purified fraction of wool fat and practically superseding it in use in England. Blended with the paraffins it constitutes unguentum alcohol lanae (ointment of wool alcohol) and with 50 per cent water it is official in the British Pharmacopoeia as unguentum aquosum (hydrous ointment). Cetyl alcohol is a white odorless waxlike solid which, when admixed with a fatty paraffin base, will emulsify water or aqueous solution in the form of water in oil emulsions. This is used to augment the action of wool fat or wool alcohols.

BAKER, Chicago

A REPORT OF THE TREATMENT OF SEVEN CASES OF GRANULOMA VENEREUM WITH PENICILLIN F BOYD TURNER, M J Australia 2 366 (Dec 1) 1945

Seven patients with granuloma inguinale that had not responded to injections of the various antimony preparations were treated with penicillin by parenteral administration and local application. Two of the patients died. Penicillin had no direct effect on the granuloma inguinale. It cleared up the secondary infection and so allowed the specific treatment with antimony to be more effective. The

Kline test elicited positive reactions in 4 and negative reactions in 3 of the cases. The positive Kline reactions were unaltered fifteen weeks after cessation of penicillin therapy.

THE TREATMENT OF FURUNCULOSIS J V DUHIG, M J Australia 2 367 (Dec 1) 1945

Favorable response and usually permanent cure were obtained in over 500 cases of furunculosis by a combination of sulfonamide drugs and an autogenous vaccine. Vaccine is used to reinforce immediate cure and to confer immunity against recurrence. The preparation of the vaccine must be made with great care. The culture should be fifteen to sixteen hours old. It should be sterilized with a 0.5 per cent solution of phenol. The vaccine contains about 20,000,000,000 organisms per cubic millimeter. Doses of 0.25 cc and 0.5 cc and a stock dose of 1.0 cc are given at intervals of five days for six to eight doses. A rest of three weeks is given, and a "booster" dose of 1.0 cc is injected.

ON THE PRICKLY HEAT FRANKLIN R FAY and ERIC SUSMAN, M J Australia 2 453 (Dec 22) 1945

A study was made of prickly heat occurring among 46 officers serving in one of the English King's Australian ships under a wartime regime in tropical waters. Twenty-six of the officers were afflicted with malaria rubra. Factors which increase the liability of a person to prickly heat are age over 30 years, fair skin, "highly strung" type of mental makeup, large intake of salt, working and sleeping below decks, high temperatures of place of work, long working hours, poorly ventilated clothing and perhaps the fact of belonging to blood group O (IV). There is no cure for malaria rubra except to leave the tropics. A healthy stoicism toward this minor illness is advocated.

FRUMESS, Denver

SOME REMARKS ON EPIDERMODYSPLASIA VERRUCIFORMIS W LUTZ, *Dermatologica* 92 30, 1946

One of two sisters who were presented in 1932 as having epidermodysplasia verruciformis or verruca plana juvenilis of a peculiar kind was inoculated with her sister's lesions, which were ground up in isotonic solution of sodium chloride. The inoculation was successful, while control tests on the patient with the solution alone gave negative results and resulted on a normal person only in transitory papular lesions.

The author states the belief that the positive reaction to the inoculation test decides the question of the diagnosis in favor of verruca plana juvenilis but that, however, a peculiar terrain is responsible for the unusual clinical picture. Is then epidermodysplasia verruciformis still a clinical entity? The author, who himself with Lewandowsky described the first case of this dyskeratosis and regarded it as a cutaneous dystrophy originating from a congenital germinal abnormality, is now inclined to consider the terrain on which the virus of the flat warts settles as unusual and different from that in cases of disseminated verruca plana juvenilis. This disposition of the skin may also be responsible for the development of malignant tumors which appear in some cases.

LUPUS ANNULARIS OF THE CERVICAL REGION SIMULATING TERTIARY SYPHILIS A ULLMO, *Dermatologica* 92 80, 1946

A man of 44 has had for the past five years on the right side of the neck a slowly growing annular lesion, which now measures 8 by 10 cm in diameter. The borderline is 0.5 cm wide, yellowish red, moderately infiltrated and not continuous. The center is whitish and scarred, it shows, however, in its middle some preserved hairs. Wassermann and Meinicke tests of the blood elicited negative reactions. Histologically, a band of infiltration occupies the papillary and dermal layers.

The infiltration consists of lymphocytes, epithelioid cells and numerous giant cells grouped in a tuberculous-granuloma-like fashion. The collagenous tissue and the elastic fibers are destroyed. The histologic picture speaks in favor of tuberculous lupus and against tertiary syphilis. The patient also has pleurisy, one significant finding is that of tubercle bacilli in the sputum. The reaction to the Pirquet test was negative; the Mantoux test in a dilution of 1:500 elicited a positive reaction. This form of annular lupus was first described by Brocq and Jacquet in 1890. The patient's general health is not impaired, although this form of cutaneous tuberculosis has been known for its virulence. Therapeutic trials with injections of mercury did not produce any significant results.

HELEN O. CURTH, New York

TREATMENT OF BURNS OF THE FACE WITH GRENZ RAYS M. BALTIM, Vestnik oftal 23 27, 1944

Baltin treated a number of burns of the face and lids of second degree with grenz rays. The effect of the treatment was noticeable in a few days, as the oozing stopped, the scales disappeared and epithelization began. One week of daily irradiation was sufficient to obtain good results.

O. SITCHEVSKA [ARCH. OPHTH.]

EPITHELIAL SYMPTOMS CAUSED BY VARIOUS DEFICIENCIES J. WALDENSTROM, Acta dermat-venereol 23 93 (March) 1942

Certain lesions of the skin and the mucous membrane are of significance in the diagnosis of idiopathic hypochromic anemia. These are (1) fissure at the angle of the mouth, (2) burning sensation of the tongue, (3) spoon nails and (4) fissuring of the skin at the finger tips. The author contends that these changes may occur in patients whose blood has normal hemoglobin value but who get an amelioration of symptoms through treatment with iron. Waldenstrom feels that in these patients there is an iron deficiency without an accompanying anemia and that the disappearance of the symptoms following treatment with iron is therapeutic proof of his suppositions. He calls this condition "sideropenia."

These same symptoms can and do occur in persons who demonstrate deficiencies in factors of the vitamin B complex, and Waldenstrom regards iron as one of the members of this complex. These symptoms which seem to be common to hypochromic anemia, and to these deficiency states, respond promptly to treatment with the vitamin B factor, which is deficient.

It becomes evident that the lesions of the skin and the mucous membrane are really not innocent and nonspecific symptoms, but are instances of widespread deficiencies which cause general impairment of cell function. When this is recognized, a troublesome condition which has persisted for years may be cured in a few weeks.

ROBINSON, Washington, D. C.

# Society Transactions

## CHICAGO DERMATOLOGICAL SOCIETY

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*April 18, 1945*

### Xanthomatous Biliary Cirrhosis with Flat Xanthomas of the Eyelids Presented by DR STEPHEN ROTHMAN and (by invitation) DR H KRYSA

L K, a white woman aged 46, noticed yellow spots about her eyes ten years ago. These spots appeared first below the eyes and a few years later on the upper eyelids. Six years ago several of these lesions were excised surgically, but more have since appeared and have grown and become confluent.

At present there are two sharply circumscribed, semicircular, slightly elevated, flat, yellow soft growths on each lower eyelid, with a sprinkle of five or six smaller lesions of similar character on each upper eyelid.

The patient gives a history of attacks of disease of the gallbladder intermittently for twenty years, with removal of gallstones in 1927 and subsequent relief from pain in the right upper quadrant of the abdomen for three years. After this, she suffered occasional attacks of severe pain in the right upper quadrant until 1938, when she became jaundiced and her stools became light and her urine dark. At that time the gallbladder was drained and removed. She suffered no further discomfort until 1940, when she again had minor attacks of jaundice and pain of short duration. In July 1944 she suffered from severe persisting jaundice, itching and severe pain.

A surgical operation performed at the Albert Merritt Billings Hospital through Dr D B Phemister's service on Dec 18, 1944, revealed no common bile duct but a bile-containing passageway in the region of the porta hepatis which was found to be an abdominal fistulous communication between the anterior wall of the common bile duct and duodenum and the right hepatic duct. A vitallium tube was inserted into the right hepatic bile duct superiorly and into the incision in the duodenum inferiorly.

The laboratory findings of interest were as follows. On Oct 20, 1944 the serum lipid level was 1,310 mg, the total cholesterol level 390 mg and the cholesterol esters content 255 mg per hundred cubic centimeters. On Feb 23, 1945, two months after the surgical intervention, the values were as follows: lipids, 1,280 mg, cholesterol, 370 mg and cholesterol esters, 305 mg per hundred cubic centimeters. The van den Bergh direct test revealed 0.5 mg and the indirect 0.8 mg of bilirubin. The amount of plasma protein levels and the albumin-globulin ratio were normal.

A biopsy of one of the cutaneous lesions was made, and the histologic section showed a typical structure of xanthoma.

### Xanthoma Eruptivum Presented by DR MICHAEL H EBERT and DR M S KAGEN

G K, a white man aged 28, presents an eruption on the extremities. The first lesions appeared on the legs about two months ago, and new ones appeared rapidly. During the patient's physical examination for induction into the Army four years ago, it was discovered that he was diabetic. He weighed 170 pounds (77 Kg) at that time. The diabetes remained untreated until recently. The patient now

weighs 123 pounds (56 Kg) He drinks moderately The cutaneous lesions have been tender to the touch but do not itch About two weeks ago a physician thought that the lesions were pyoderma and administered a course of penicillin and sulfonamide compounds, without effect The lesions are most numerous on the legs, especially over the calves, on the lateral and posterior surfaces of the thighs and on the buttocks, but they are also present on the elbows and the arms When the patient was admitted to the hospital, the blood sugar content was 144 mg per hundred cubic centimeters and the blood pressure was 140 systolic and 54 diastolic He has been receiving 140 units of insulin per day for the past week and is still excreting sugar in the urine The total cholesterol level of the blood serum was 500 mg per hundred cubic centimeters

The lesions are of two types 1 There are raised, flat-topped, dull red papules varying from the size of a matchhead to that of a split pea At present these are covered with adherent grayish crust scales When the patient was first seen, one week ago, the lesions were inflammatory, many were surrounded by a bright red halo, and many of the crust scales were dark colored On removal of the scales, however, there was no pus When the skin was stretched with the fingers, the lesions had a distinctly yellow color 2 There are pinhead-sized light yellow papules scattered among the other lesions and especially numerous on the buttocks

In a histologic section taken from what appeared to be the center of a papule there was decided acanthosis, with a papillomatous folding of the outer portion of the epidermis The spaces between the folds and the surface were covered with a nucleated crust scale containing a dried microabscess The elongated papillae and the area below the epidermis were infiltrated with foam cells In sections taken from other areas the foam cell infiltrate was in the midcorium, in the neighborhood of a hair follicle In frozen sections stained with sudan III one sees small and large lipid granules These are most numerous in the foam cells of the infiltrate and in the reticular cells of the small vessels of the papillae

#### DISCUSSION OF THE TWO PRECEDING CASES

DR CARL W LAYMON, Minneapolis Thannhauser, Magendantz, and Montgomery and Osterberg have pointed out the differences between xanthoma of the tuberous type and that of the disseminate type Xanthoma of the palms and the soles occurs more frequently in xanthoma tuberosum and is especially frequent when hepatic disease is present Lesions of the lids can be present in either the disseminate or the tuberous type

DR S W BECKER I wondered how the diagnosis of biliary cirrhosis had been made I did not see a note as to the operative findings I agree with the diagnosis of xanthelasma

DR THEODORE CORNBLEET The cholesterol content of the blood was not reduced in the two months following operation, when presumably the bile from the liver could empty into the intestine During this period also there was no regression of the lesions In another patient that I followed, there were multiple xanthomas, high values for blood lipids and jaundice After an operation the jaundice gradually disappeared, but the levels of lipids in the blood remained unchanged It would seem that the elevated values for fatty material are not explained by simple mechanical means The deposits in the biliary system and in the skin would seem to depend on a common factor or factors When deposits blockade the free flow of bile and result in jaundice, the disease is secondary then and not primary to the xanthomatous state

DR ARTHUR C CURTIS (by invitation), Ann Arbor, Mich The first case was interesting because the patient had hyperlipemia Dr Hamilton Montgomery has previously emphasized the frequency of hyperlipemia and xanthelasma Hyperlipemia appears in association with xanthelasma in 75 to 80 per cent of the cases In a series of patients with xanthelasma, studied not long ago, the same incidence of hyperlipemia was found The liver is the storehouse for fat as well as the store-

house for glucose. The relationship of choline and choline-like substances to the mobilization of hepatic fat has been studied considerably. However, in most of the cases of xanthelasma in which the blood fat contents were determined and tests of hepatic function made, I have been unable to prove any actual hepatic damage. The patient seen today with xanthelasma has a congenital absence of the common bile duct. In the past there must have been a considerable amount of fat stored in the liver, and, according to the laboratory data, two months after operation there still is an enormous amount of circulating blood cholesterol.

Several years ago Dr John Sheldon and I reported on the study of such a patient. A young man with diabetes had a rapid onset of xanthomas and then later suffered diabetic coma. During this period he had hyperlipemia, the blood lipid content being 12 per cent, and xanthoma diabetorum. He was given a high carbohydrate diet and insulin. The hyperlipemia disappeared, and the blood fats returned approximately to normal levels. The amount of insulin was then slowly decreased. As acidosis began to develop, the hyperlipemia recurred and we allowed him to return to a mild diabetic coma. At that time the blood fat content had again risen to more than 6 per cent. His xanthomatous lesions disappeared during the period when the blood fat levels were normal. We did not maintain his hyperlipemia long enough to get a reappearance of the xanthomatous lesions.

DR RUBEN NOMLAND, Iowa City. I had an opportunity to study 3 patients with damage to the liver and the development of xanthomatous lesions associated with this damage. Two of them had obstruction of the common bile duct with prolonged jaundice, with decided increase of the blood fat and cholesterol levels. One of the 2 had xanthelasma and the other a widespread mixed type of both flat and tuberous xanthomas. The third patient had prolonged jaundice over a great many years and had tuberous lesions mostly. At operation nothing was found to explain the long-continued jaundice, and the patient had no obstruction to the bile ducts. She had enlarged glands in the retroperitoneal area and xanthomatous infiltration of these glands and of the gallbladder.

I think that damage to the liver with prolonged jaundice occasionally disturbs the metabolism of cholesterol and other lipids, with the development of hyperlipemia and similar states and the subsequent formation of xanthomatous deposits in the skin in the form of either flat or tuberous xanthomas.

DR STEPHEN ROTHMAN. If I understood Dr Laymon correctly, he said that xanthomatous biliary cirrhosis is always connected with the tuberous form of cutaneous xanthomatosis. This is not borne out in the literature (see Thannhauser, S. J. *Lipidoses*, in Christian, H. A. *Oxford Loose-Leaf Medicine*, New York, Oxford University Press, 1940, vol 4, pt 1, pp 3-365). In answer to Dr Becker's question, the association of xanthomas with hypercholesteremia, persistent jaundice and a large cirrhotic liver is well known to be a distinct form of primary essential xanthomatosis. It is true that in our case at operation no xanthomatous infiltration was seen in the bile ducts, but it is also true that in the liver the nests of xanthoma cells ultimately undergo destruction and scar tissue develops. Xanthomatous biliary cirrhosis is the manifestation of a primary systemic disease of histiocytic elements. High lipid values as well as xanthomatous obstructive infiltration of the bile ducts and xanthomas of the skin, blood vessels and other parts of the body are due to this systemic disease. It is not to be expected that after release of the biliary obstruction the lipid values of the blood will change. Generalized intensive pruritus is rather common in this disease.

**Urticaria Pigmentosa with Bullae.** Presented by DR LOUISE E. TAVS (by invitation).

M. L., an infant, had an eruption at the age of 2½ months. It appeared first on the abdomen but subsequently involved the legs and the back. When the infant was 9 months old the scalp became involved with oozing and crusting, and the occurrence of bullae was noticed first when the infant was 5 or 6 months old.

Simultaneously with the involvement of the scalp numerous bullae appeared. Remissions occur with rapid exacerbation within a few hours. Pruritus has been moderate. The patient had one episode of generalized intense flushing of the uninvolved skin with paling of the lesions lasting for five minutes.

The mother and maternal grandmother are said to have migraine headaches. A paternal great-aunt had eczema. One paternal cousin has a "birth mark" involving the leg, and another was born with "brown patches."

The patient's past history reveals that she had chickenpox one month ago. She has not been vaccinated but has received immunization therapy for diphtheria and whooping cough.

Examination of the patient at present reveals oval discrete yellowish brown and reddish brown nodules, some with peripheral erythematous zones. There are also pigmented macules, and previous examinations showed bullae varying in size up to a dime, which were tense and filled with serous fluid. The lesions are present on the scalp, the lateral aspects of the cheeks, the neck, the torso and the extremities, and Darier's sign is positive.

The blood cell count revealed the hemoglobin content to be 70 per cent, erythrocytes, 3,950,000, and leukocytes, 15,400, with a differential count of 39 per cent neutrophils and 61 per cent lymphocytes. The blood cholesterol level was 170 mg per hundred cubic centimeters of serum. The urine was normal.

A biopsy was performed on a bullous lesion of the left arm. A histologic examination of a section showed slight edema of the epidermis. The papillae were edematous, and just below them there was a densely packed band of cellular infiltration from which linear strands of cells extended downward. The polychrome methylene blue stain showed many of these cells to be mast cells. Staining with sudan III showed a considerable amount of fat in the subpapillary band and in the vertical cellular strands.

The patient has had no treatment up to the present.

#### DISCUSSION

DR CLARK W. FINNERUD: Years ago I reviewed the literature on urticaria pigmentosa. Though I have forgotten the frequency of occurrence, one of the rarest manifestations was xanthoma-colored lesions. The rarest manifestation was bullae. These rare features were well illustrated in this patient.

DR S. W. BECKER: I was impressed by the fact that the regions in which the bullae had appeared were edematous, as though the child had been scratching or some one had rubbed them.

DR MARCUS R. CARO: Another remarkable feature in this case is the histologic picture. Staining for fat with sudan III showed a considerable amount of fat in the corium. On going over the literature on urticaria pigmentosa, I was amazed at the number of cases in which the lesions were described as being xanthoma-like, but in none of them could I find that fat was demonstrated. The presence of fat as well as bullae makes this case unusual.

**Striae Distensae** Presented by DR CLEVELAND J. WHITE

D. S., a girl aged 14, noticed some "peculiar" lines on the upper portion of the thighs and buttocks about six weeks ago. A physical examination at that time showed a healthy-appearing young girl with many linear striae of glistening appearance symmetrically distributed over the areas mentioned. There have been no recent illnesses. All the laboratory examinations have so far revealed no abnormalities, and a roentgenologic examination showed that the sella turcica is normal. The tonsils are large and apparently infected.

The patient is presented because of the apparent idiopathic appearance.

#### DISCUSSION

DR FRANCIS E. SENEAR: The girl said something that was not in the history that she had gained 15 pounds (7 Kg.) in the last year. That might be an explanation for the development of the linear striae.

DR S W BECKER I questioned her about the gain in weight She said that she had gained 15 pounds, which settled in the involved regions

DR MAURICE OPPENHEIM (by invitation) One of the interesting features is that the striae distensae are present in such a young girl One can see women who have given birth to many children without a trace of striae, on the other hand, one can find numerous striae gravidarum in women who have had one abortion Striae distensae can be caused by conditions like typhoid, meningitis and tuberculosis, mostly after a long rest in bed, and are not due only to a rapid growth in the length of the body As I stressed in my articles, there are two factors present first, a congenital weakness of the elastic fibers and, second, some toxic or endocrine influence which causes these striae distensae They are not always perpendicular to the direction of growth They are without doubt due to a congenital weakness of the elastic fibers, as in other cases of cutaneous atrophy Growth alone or hypertension alone does not cause striae (Oppenheim, M Atrophy of the Skin, in Jadassohn, J Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1931, vol 8, part 2)

DR MICHAEL H EBERT Some years ago I reported 2 cases of hypertrophic striae in young women Since then Dr Ormsby and I have observed several such cases, and sometimes considerable mental disturbance is caused to the mother as well as to the child In the hypertrophic type the lesions stand out instead of being depressed Histologically, there is not only a disturbance of the elastic tissue but also an inflammatory reaction If these cases are followed for a number of months, the lesions are found to subside eventually I agree with Dr Oppenheim that not all these conditions are on an endocrine basis That is well illustrated by tumors of the adrenal glands and other endocrine tumors associated with an increase in weight and blood pressure which cannot be explained on the basis of tension alone This condition is even more evident in the hypertrophic lesions of adolescence, which are not common but which do occur

DR STEPHEN ROTHMAN The obvious cause of these striae distensae has been that the patient gained 15 pounds in a short time I wonder if the endocrinologists are right when they emphasize that in the Cushing syndrome the striae are purplish The color of striae obviously depends on the state of the venous circulation, and I saw purplish striae in cases like the one presented without any evidence of Cushing's syndrome

DR ARTHUR C CURTIS (by invitation), Ann Arbor, Mich I do not think that the color of the striae is of diagnostic importance in Cushing's syndrome I have seen purple striae in patients who did not have Cushing's syndrome

DR CLEVELAND J WHITE I did not get an accurate history of the onset from either the mother or the patient The latter had had acute tonsillitis, and I wondered if the enlarged tonsils might be a factor

**Erythema Induratum (Bazin)** Presented by DR STEPHEN ROTHMAN and (by invitation) DR A L SHAPIRO

D J M, a white man aged 44, a cattle buyer, was first examined in the University of Chicago Clinics on Aug 12, 1943, when a diagnosis of far advanced tuberculosis of the lungs was made In November and December 1943 he had a three stage thoracoplasty, after which he has gradually improved so that he is now able to work regularly In September 1944 there developed the dusky red, firm, slightly tender, cutaneous-subcutaneous node now present on the calf of the right leg There has been only a small increase in size since its onset Lateral to this lesion the patient also presents an atrophic depressed scar, a residual of a similar erythematous lesion which appeared several months previous to the present infiltrate and which healed spontaneously after a few months' duration

Previous to the thoracoplasty his sputum gave positive reactions for tuberculosis (Gaffky scale, III or IV) All the many specimens examined after the operation failed to yield tubercle bacilli On August 16, a guinea pig was inoculated with

sputum, and it was found to have no tubercle bacilli when killed on October 18. The Wassermann and Kahn reactions of the blood were negative on Aug 22, 1943. There are no recent laboratory reports available on the blood or urine. A roentgenogram of the chest on Sept 15, 1944 showed no sign of tuberculous activity.

A histologic examination of a section taken from the cutaneous lesion showed defined areas of infiltration in the lower part of the dermis and in the subcutis, consisting of lymphocytes and epithelioid cells. Many of the infiltrates were around thickened blood vessels. There was an unusually large number of leukocytes also.

#### DISCUSSION

DR LOUIS H WINER, Beverly Hills, Calif. I was interested in the histologic section because there was none of the proliferation that is seen in erythema nodosum, namely, a proliferation of the leukocytes around the vessels. In this patient the subcutaneous fat was undergoing a liquefaction necrosis, and it seems as though the adjacent cells contained phagocytic remnants of this fat. Therefore, I offer a diagnosis of nonsuppurative panniculitis in this case.

DR M J REUTER, Milwaukee. I did not see the sections. Dr Winer brought up the question of inflammatory infiltration of the subcutaneous fat tissue. I have always felt that this was one of the characteristics of erythema induratum.

#### Blastomycosis Presented by DR MAURICE OPPENHEIM (by invitation)

E G, a white man aged 46, first noticed a small pustule below the left eye in November 1944. Other pustules appeared in the periphery. Various ointments were applied without result. The pustules finally became coalescent. An operation was performed, and finally six roentgen ray treatments were given, altogether 1,500 r being used. Since no improvement was observed, he was referred here for further observation and treatment.

A physical examination reveals an oval elevated new growth of skin 0.5 cm below the left eyelid, 3 cm long and 2 cm wide. The surface is cauliflower-like, covered partially with crusts. The color is gray, and the center is depressed. The surrounding skin of the inner margin of the tumor-like growth is dark red and shows small yellow pustules, partially superficial and partially deeper. This surrounding inflammatory area is small and sharply defined against the normal surrounding skin. The growth is hard, finger pressure is not unduly painful, and there is no spontaneous pain. The lymph nodes in the preauricular area are not enlarged.

The smear of material from the pustules showed few double-contoured large bodies with a granular protoplasm; no budding forms were seen.

The blood cell count showed a hemoglobin content of 95 per cent, erythrocytes, 4,800,000, and leukocytes, 10,000, with a differential count of 45 per cent lymphocytes, 2 per cent monocytes, 53 per cent leukocytes and no eosinophils; the color index was 0.9. The Kahn reaction of the blood was negative.

The biopsy section taken from the margin revealed a wartlike growth with acanthosis, hyperkeratosis, parakeratosis, horn pearl formation and papillae growing in every direction. One part of the histologic section showed ulcerations with lymphocytosis and many leukocyte elements. The base of the ulcerated area was formed of round cells and many plasma cells mixed with giant cells of the Langhans type. The papillary layer, the subpapillary layer and the reticular layer of the cutis were infiltrated with lymphocytic elements, with many plasma cells and few giant cells. In some of the giant cells of the ulcerated area double-contoured, round corpuscles with a granulated protoplasm were visible; budding forms were also present.

Intracutaneous tests with trichophyton and oidiomycin elicited strongly positive reactions.

Treatment with potassium iodide, 10 Gm in 180 cc of water, was started, the patient taking 1 tablespoon daily, the dosage being increased to 5 tablespoons a day, or about 5 Gm. The lesion shows decided improvement. No organisms could

be found in the last smears of material from the small abscesses, which have diminished in number

#### DISCUSSION

DR HARRY M HEDGE There was a similar case at Northwestern University some years ago, the patient being a Negro porter. He had lesions on both cheeks and on the hands and two lesions on the buttocks. Large doses of potassium iodide were tried, and the patient got better and then worse interchangeably. Finally, a special electrode was made for the electric cautery, and with a broad, straight wire these lesions were cut off until they bled profusely. The lesions healed well, with little scarring. The lesions on the buttocks were about 10 cm in diameter, the one on the hand 13 cm and the one on the cheek a little smaller.

DR MAURICE OPPENHEIM (by invitation) I think that this case deserves a little more discussion because the disease is one of the local types of blastomycosis of the American type on account of the location, close to the eye. I was the first one to present in Vienna, Austria, in 1903, a case of local blastomycosis of the American type (Lowenbach, G, and Oppenheim, M. *Beitrag zur Kenntnis der Hautblastomykose, Arch f Dermat u Syph* 69 121-144, 1904). Later 4 cases of a local type of blastomycosis could be observed at the Neumann and Finger clinic in Vienna (Internationale Congresso di Dermatologia e Sifilografia, Roma, April 8-13, 1912). (See also Oppenheim, M. *Die Hautblastomykose, Wien med Presse* 46 869-879, 1905.)

**Mycosis Fungoides** Presented by DR HERBERT RATTNER and (by invitation) DR H H RODIN

H C, a Negro aged 56, was admitted to the dermatologic clinic of the Cook County Hospital on April 5, 1945, with the complaint of a generalized pruritic eruption of about eighteen months' duration. He stated that he was in good health until November 1943, when an itching eruption in the scalp developed, which failed to respond to local treatment. Within a period of five months the eruption spread across the face and over the entire body. At the onset the pruritus was severe enough to interfere with the patient's sleep, but in the past few months he has been sleeping better after receiving injections which "made him feel hot." At present he is able to sleep well, and in general he feels well. He stated that tests of the blood for the past five years, taken as a preemployment requirement, have given normal results.

His past history is essentially irrelevant, with the exception of the usual childhood diseases. He had smallpox about 1905 and gonorrhea in 1935.

The presenting dermatitis consists of a generalized eruption composed of areas of hyperpigmentation, numerous oval and circinate infiltrated plaques from the size of a quarter to that of a dollar, composed of lichenoid papules, and several walnut-sized to egg-sized, round, smooth tumors located over the right scapular and lumbar regions.

The serologic reaction of the blood was negative.

#### DISCUSSION

DR EDWARD A OLIVER It is now realized that mycosis fungoides among Negroes is not so rare a condition as formerly thought. Several months ago at a meeting of this society I showed a Negro with generalized exfoliative dermatitis with the microscopic diagnosis of lipomelanotic reticulosis. This patient now has typical mycosis fungoides.

**Melanodermatitis (Occupational)** Presented by DR OTTO H FOERSTER and DR HARRY R FOERSTER, Milwaukee

The patient first noticed lesions on the dorsa of the forearms a year ago as red itching elevations. He squeezed a waxlike substance out of some of these and did not observe vesiculation. The lesions increased in number and extent, fusing in

places to form patches. A brownish discoloration was first observed four months ago, at which time the eruption had extended over the forearms to the flexor surfaces of the elbows, with a few lesions above the elbows and on the dorsal surfaces of the hands. In July 1944 he observed on the cheeks small red spots, which increased in size and number to form large red blotches that became brownish several months later. The eruption was most pronounced on the cheeks and about the jaws and extended to the forehead and the neck a month ago. A few inflammatory nonpigmented patches appeared on the legs several months ago.

The patient is now employed as supervisor of a tool-grinding room, where he works from ten to twelve hours a day in a dusty atmosphere. There has been exposure to lubricating and cooling oils, carbide dust and emery dust for three years, and since the dermatitis developed he has observed severe smarting and burning sensations when a mixture of dust and oil gets on his face. There is no history of exposure to pitch or tar. There has been no medication, and the dermatologic and medical histories are otherwise irrelevant. The only cosmetic used has been a shaving cream.

The patient presents a diffuse and patchy eruption of macules and lichenoid and follicular papules with chronic inflammation and intense pigmentation. The lesions are confined to the face, neck, upper extremities and legs. There are no lesions of the mucous membranes. Otherwise the physical examination revealed nothing abnormal. The blood pressure is 100 systolic and 80 diastolic.

The blood cell count and the urine were normal. Patch tests made with seven samples of materials to which the patient is exposed at work showed no distinctly positive reactions. The blood cell count showed a hemoglobin content of 85 per cent, erythrocytes, 4,860,000, and leukocytes, 12,400, with a differential count of 2 per cent stab cells, 38 per cent lymphocytes, 2 per cent eosinophils, 2 per cent monocytes, 1 per cent basophils and 55 per cent neutrophils.

The histologic examination of a section from one of the lesions showed hyperkeratosis and parakeratosis with follicular plugging, a well developed stratum granulosum epidermidis, a thinning of the rete and edema and disintegration of the interpapillary pegs. There was pronounced edema of the papillary and the subpapillary layers with a well developed cellular infiltrate, predominantly lymphocytic, diffuse in some areas but chiefly perivascular. The capillaries were dilated and edematous. There was a dense lymphocytic infiltrate about the deeper vessels and cutaneous glands. There were no plasma cells.

#### DISCUSSION

DR H. E. MICHELSON, Minneapolis. I think that this is an interesting case and offers much opportunity for speculation. One thing that strikes me in all patients with lichen planus and lichen-planus-like eruptions is the tendency toward pigmentation. There must be something causing these eruptions that stimulates production of pigment. Undoubtedly when due to bismuth and arsenic this disease is more aggravated.

DR HARRY R. FOERSTER, Milwaukee. I thought this case sufficiently interesting to present because of the intense melanosis of the face. If that were the only condition present, a differentiation from poikiloderma of Civatte would be suggested. There was reticulation in the arrangement of the pigmentation on the face as well as lichenoid dermatitis, particularly on the forearms. In industry most of the eruptions are associated with exposure to pitch or tar and to sunlight. In this instance the dermatitis developed on the forearms and the face originally, apparently as an oil folliculitis. The pigmentation has not been so pronounced on the arms at any time as on the face. The dermatitis first developed in July, but the patient had not been working out of doors at the time. He said that whenever a mixture of emery or graphite, shop dirt and oil contaminated his skin he observed intense smarting and irritation, suggesting dermatitis as the first manifestation.

In this case there were features suggestive of lichen planus and also a form of lupus erythematosus, but the histologic examination serves to rule out both these

diseases and the history favors an occupational and external cause. A similarity to melanodermatitis lichenoides and melanosis of Riehl is suggested, particularly by the facial eruption. A systolic blood pressure of 100 might suggest the possibility of an adrenal factor in the predisposition to pigmentation.

**Idiopathic Multiple Hemorrhagic Sarcoma (Kaposi)** Presented by Dr S J ZAKON

A G, a Jewish man aged 72, born in Rumania, states that he began to notice red blotches on his hands about eight months ago. There were no objective symptoms. His general health is fair, and he is convalescing from a herniotomy. He is a watch repairer by trade.

An examination on April 16, 1945 revealed reddish brown and bluish red discrete nodules and plaques on the dorsa of the hands, the extensor and flexor aspects of both forearms, the outer aspect of the right thigh, the tip of the nose and the lower lip, involving the vermilion border. Lesions were also present on both legs, on the dorsal aspect of the second toe of the left foot and on the large and third toes of the right foot. These lesions apparently were of much longer duration.

DISCUSSION

DR THEODORE CORNBLEET: There were nodules on the tongue which I presumed to be similar to those on the skin. This would be the first example that I have seen of such lesions on the mucosa.

**Unexplained Fluorescence Phenomenon** Presented by Dr THEODORE CORNBLEET and Dr H C SCHORR

O T, a married Negro woman aged 40, has had a lesion on the left calf for some time. This is polycyclic in character, subacute without subjective sensations. Examination under the Wood light revealed fluorescence, most evident on the right leg, especially on the anterolateral surface. This fluorescence had two qualities: a central zone that was more intense and yellowish and, surrounding this, a more diffuse zone, with outlying islands for some distance beyond, brilliantly white. The fluorescence was less evident on the left leg but absent over and near the lesions. Scales were removed and examined, and they fluoresced (white). The same scales were observed directly for fungi, but none were found.

The patient works in a bakery and uses a goodly amount of yeast in making large quantities of dough. She says that she does not take medicines. No applications were made to the affected areas. The serologic reaction of the blood was positive.

DISCUSSION

DR THEODORE CORNBLEET: This woman gave no history of putting petrolatum on her legs. I questioned her again, and she maintained that she had not used petrolatum for the last nine months. An area which was swabbed with purified benzene U S P continued to impart its fluorescence.

DR EDWARD A OLIVER: Often on examining children's scalps one will find fluorescent particles, probably due to soap around the neck or in the ears. I do not think that that situation is unusual.

DR THEODORE CORNBLEET: I have no explanation to offer for this phenomenon. I do not think that it is remarkable. I have been using the Wood light in examining many skins, and once in a while I find fluorescent particles. In my experience, however, it is not common to find cutaneous fluorescence similar to that found in this case. The pattern in this case has been more or less the same. It probably will be found that some extraneous substance is causing the fluorescence. Porphyrins do not behave this way. There is nothing in this woman's history or examination otherwise that would give a lead for association. Otherwise one might look for other patients with similar histories to see if they have such phenomena of fluorescence.

Disseminated Subacute Lupus Erythematosus (?) Presented by DR STEPHEN ROTHMAN and (by invitation) DR Z FELSHER

P R, a white woman aged 34, was first seen in the metabolism clinic of the University of Chicago Clinics on Nov 22, 1944. At that time she complained of generalized weakness, glandular swelling and painful joints of one year's duration. For the past year she had also had attacks of cyanosis of the fingers in cold weather. There was also a history of several attacks of "pleurisy" since Easter 1944. The patient was admitted to the Albert Merritt Billings Hospital on Dec 4, 1944 and remained there until Jan 5, 1945. A physical examination revealed generalized emaciation, discrete, large, firm lymph nodes of the neck, and enlargement of the left ventricle, with systolic murmurs at the base and the apex. The fingers showed erythematous patches on all terminal phalanges surrounding the finger nails but nothing around the toe nails.

The agglutination test for *Brucella* gave negative results. Histologic study of a section taken from a lymph node showed only hyperplasia and some fibrosis. Cultures of the blood were sterile. A catheterized specimen of urine showed a few red blood cells, a few hyaline casts and a few white blood cells. The blood chemistry showed a normal value for nonprotein nitrogen. The blood cell count showed a hemoglobin content of 9.5 Gm and an erythrocyte count of 3,200,000, the leukocyte count ranged from 4,600 to 7,000 during the patient's stay in the hospital. The differential blood cell count was normal. The Wassermann reaction was anticomplementary, and the Kahn reaction was negative. A roentgenogram of the chest revealed that the heart was 15 per cent oversized, the pulmonary fields were clear and there were no adhesions. An electrocardiogram showed a deviation of the right axis, with other findings within normal limits. A roentgenogram of the fingers showed mild periarticular osteoporosis.

The results of the sternal puncture were noncontributory. No evidence of amyloid disease was established by the congo red test. Normal hepatic function was indicated by the hippuric acid test. The urine concentration test showed normal renal function, but the urea clearance test showed slight impairment. The chemical examination of the blood revealed a total plasma protein content of 10.05 mg per hundred cubic centimeters, the albumin-globulin ratio was reversed (0.55), the albumin content being 3.58 Gm per hundred cubic centimeters and the globulin 6.47 Gm.

A biopsy was performed on a specimen from a finger, and a histologic section revealed a normal epidermis, fibrotic connective tissue in the upper corium and collagen degeneration in the midcorium and deep corium. There was no atrophy of the sweat glands.

#### DISCUSSION

DR FRANCIS E SENEAR: I thought that it was rather interesting to contrast this patient with the one shown in the Cook County Hospital who had definite involvement at the nail fold posteriorly. The patient shown today had such exaggerated lesions along the lateral nail folds. On three fingers of the left hand, on the ulnar side particularly, she had lesions of that type.

DR LOUIS H WINER, Beverly Hills, Calif: The histologic picture is not that of lupus erythematosus, because it lacks the islands of lymphocytic infiltration seen in this disease. On an examination of the cutis histologically one sees that the vessels are disintegrated much as in periarteritis nodosa. In periarteritis nodosa the larger blood vessels are also involved, whereas in this case they are only the small vessels. I have never seen anything exactly like this microscopically, but I cannot offer a diagnosis.

DR FRANCIS E SENEAR: I should like to ask Dr Winer if in some cases of periarteritis nodosa one does not find involvement of the small vessels as well as the large ones.

DR LOUIS H WINER, Beverly Hills, Calif: Some months ago Dr Michelson and I showed a case to this society in which the small vessels were involved.

DR ARTHUR C CURTIS (by invitation), Ann Arbor, Mich I certainly do not know of any quick or rapid method of curing lupus erythematosus of the acute type When a patient presents an acute lesion such as this woman does, the prognosis should be guarded I know of no way of telling whether the disease will become subacute or disseminated It is my experience that in many cases of this type the disease becomes worse, disseminated lesions develop and the patient dies

The organism found in the blood of a patient with acute disseminated lupus erythematosus, sent to me by Dr Mitchell, was identified as a pleuropneumonia-like organism To date no one has described this organism as being an etiologic factor in human disease It has been described as occurring in animals, and investigators interested in rheumatoid arthritis have been able to produce a form of arthritis in animals with this organism I have taken a few specimens of blood from my own patients with lupus erythematosus but have been unable to obtain a similar organism The appearance of this bacterium in the specimen sent to me by Dr Thompson and Dr Mitchell may have been a contaminant, or my inability to grow it may have been due to the mediums used

DR EDWARD A OLIVER Inasmuch as the internists are taking so much interest in lupus erythematosus of the disseminated type, I should like to ask Dr Curtis whether he would like to discuss the work of Dr Rich and his associates at Johns Hopkins Hospital on lupus erythematosus and periarteritis nodosa

DR ARTHUR C CURTIS (by invitation), Ann Arbor, Mich I imagine that many of the members heard Dr Rich when he talked before the Chicago Medical Society two months ago His conception of the cause of periarteritis nodosa is that of a hyperergy produced by certain things, such as a foreign protein or a sulfonamide drug The latter may explain the increase in periarteritis nodosa

Lupus erythematosus and periarteritis nodosa are being diagnosed by internists oftener than they have been in the past This may, I think, be due to awareness of the diseases, for Osler said that "the incidence of a disease in any community is in proportion to the acuity of the doctors in that community"

DR S W BECKER In line with the remarks of Dr Winer, when I examined the patient I noted that the lesions were telangiectatic rather than inflammatory, as in lupus erythematosus There is a group of telangiectatic lesions associated with infection The patient could have a generalized infection which produced the arthritis and the telangiectasia I do not believe that a diagnosis of acute lupus erythematosus can be made from the clinical picture presented today

DR STEPHEN ROTHMAN In the histologic section presented the collagen degeneration is definite and indicates lupus erythematosus I am unable to comment on the changes in the vessels Periarteritis nodosa is a highly improbable diagnosis because clinically there is no nodule formation and the blood does not show eosinophilia The low white cell count and the reversed albumin-globulin ratio are in favor of lupus erythematosus Telangiectases could be seen around the nails from time to time

Heat and Emotional Urticaria Presented by DR STEPHEN ROTHMAN and (by invitation) DR R E GREEN

M H, a white woman aged 36, was first seen in the dermatologic clinic of the University of Chicago Clinics on April 6, 1945 Her complaint was that for the past ten years "hives" developed all over her body whenever she was subjected to heat, physical stress or an embarrassing situation The illness began when the patient became excited about diving off a high board She finally dived, and she noted hives on coming out of the water Since that time, except for some slight variations in intensity, she has experienced similar attacks, always preceded by a pounding heart and a flushed face, whenever she takes a hot bath, goes from a cold to a hot environment, exercises or feels embarrassed One summer she was free from attacks after exposing herself to the sun for considerable periods early in the season In the following seasons, however, sun baths were unsuccessful in suppressing the attacks This patient is not an emotionally labile person

A general physical examination revealed no essential abnormalities, and the laboratory findings were noncontributory. An injection of 0.1 cc of a 1:1,000 solution of mecholyl chloride produced a decided wheal in this patient, whereas in control patients there was no whealing present. The patient was given a hot bath at a temperature of 46.5 C for five minutes, and generalized urticaria consisting of densely distributed wheals 2 to 3 mm in diameter and diffuse erythema immediately developed. Areas not immersed in the hot water were equally involved. There was no change in the blood cell count or the cell volume during this test. Radiant energy (the patient remained in a sweat chamber with a temperature of 59 C for one hour), ultraviolet rays, infra-red rays and 0.5 mg of neostigmine methylsulfate given subcutaneously failed to cause urticaria. By comparison of the sweating reaction of this patient with those of normal patients in the heat chamber and in the acetylcholine test, it was found that the patient's sweating activity was greatly decreased.

Passive transfer of the heat sensitivity by the Prausnitz-Kustner technic could not be accomplished.

The patient has been given daily intradermal injections of mecholyl chloride in an attempt to desensitize her. Although the urticarial response to these injections is still great, she notices a subjective improvement and is now able to take long walks with no urticaria resulting, formerly an impossibility.

The urticarial reaction to acetylcholine bromide 1:1,000 is demonstrated on the patient's arm.

#### DISCUSSION

DR CLARK W. FINNERUD: I should like to ask Dr. Rothman if he has had any success in treating light allergy or cold allergy by this or any other method.

DR STEPHEN ROTHMAN: On record I have 3 female patients with emotional and heat urticaria. Two responded well to desensitization with acetylcholine. They were young, light blonde, poorly pigmented Scandinavian girls in whom emotional stimuli caused most trouble. The patient presented today is a well balanced person who does not become excited easily. Her urticaria in most instances is elicited by heat stimuli. She gets emotional urticaria only in situations which make her blush.

(I want to add that the improvement after the administration of mecholyl chloride proved to be only temporary in this case. I did not succeed in desensitizing the patient to acetylcholine.)

**Lichen Nitidus** Presented by DR STEPHEN ROTHMAN and (by invitation) DR D. J. NIEDERMAN

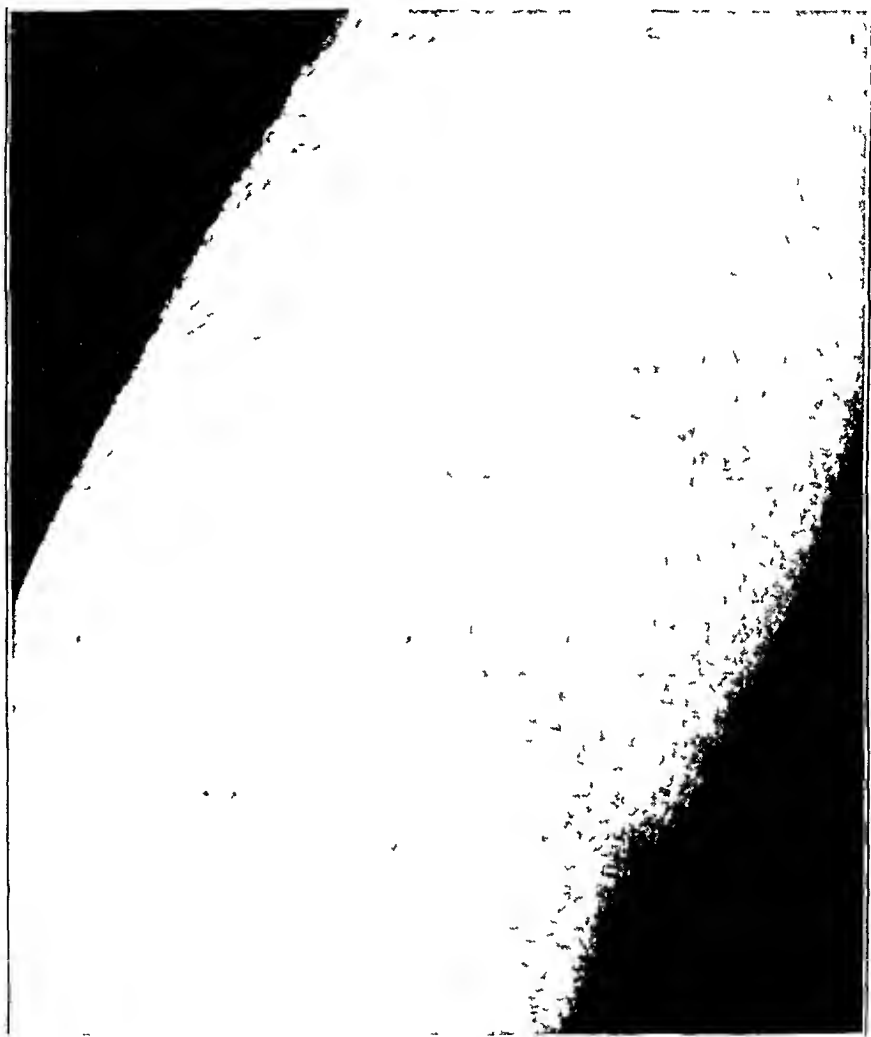
D. B., a white boy aged 6 years, was first seen in the dermatologic clinic of the University of Chicago Clinics on March 26, 1945 with a history of having had a rash on his forehead, legs and arms for three months with no subjective symptoms. Six months before his visit to the clinic the family moved into an apartment where a woman had just died of tuberculosis. The family lived there for three months, and the rash was first noticed at the time of moving out of this apartment. The patient was born in a mining community in Kentucky, where the milk may have been unpasteurized. The child has apparently been in good general health except for continuous colds for one year. His past history reveals measles at the age of 4 years and impetigo one year ago. He has just recovered from chickenpox.

A physical examination revealed enlarged, infected tonsils, carious teeth, a mucous discharge and obstruction of the nose and moderately enlarged, freely movable lymph nodes in both axillae. Fluoroscopic and roentgenologic examinations showed a normal chest. The mother's chest also was normal on fluoroscopic examination.

Tuberculin tests were performed on March 29 and April 17, 1945, with an intradermal injection of old tuberculin in a 1:1,000 dilution, the reaction was negative. Gastric lavage washings were inoculated into guinea pigs yesterday.

Examination at present reveals pinhead-sized globular or semiglobular lichenoid papules with shiny surfaces arranged in groups on the forehead, face, trunk and extremities, with no characteristic distribution. The genital region is free.

A histologic study of a section taken from the lesions revealed a normal epidermis except above the infiltrates, where it was compressed to a thin plate with destruction of its lower surface. There were two sharply circumscribed round superficial infiltrates pressing hard against the epidermis. They consisted



Lichen nitidus

of lymphocytes, epithelioid cells, fibroblasts and giant cells. One of the infiltrates surrounded a follicular infundibulum, the other did not. There was a slight perivascular infiltration of the subpapillary plexus. The connective tissue was normal.

#### DISCUSSION

DR H. E. MICHELSON, Minneapolis. Lichen nitidus when first described was considered a localized disease. Since then patients with generalized eruptions have been reported, especially by the English dermatologists. For my own part, I do

not believe that lichen nitidus has anything to do with tuberculosis, but I think that more studies on vitamin A should be made

DR MAURICE OPPENHEIM (by invitation) The disease is not tuberculosis. I believe that it belongs to some nevroid type of lichen

DR STEPHEN ROTHMAN This case illustrates beautifully the fact that histologically a tuberculous structure does not necessarily mean tuberculosis. The negative reaction to tuberculin in this child can be taken as definite proof that he has no tuberculosis. I wonder if lichen nitidus in general has anything to do with tuberculosis

**A Case for Diagnosis (Neural Leprosy?)** Presented by DR CLEVELAND J WHITE and (by invitation) DR D E MEIER and DR S E RAVITZ

A single, deaf-mute woman, aged 35, was born in Alabama and lived in Alabama and Mississippi until 1940, when she came to Chicago. Her father died at the age of 59 of cerebral hemorrhage. Her mother is living and well. The patient had the ordinary diseases of childhood and meningitis at the age of 4, resulting in deafness. The menstrual history is noncontributory.

The present complaint began when the patient was 12 years old, when she noticed a small itching spot about the size of a quarter on the right thigh. The spot slowly enlarged, and new ones began to appear on other parts of the body below the waist line. The lesions vary in size. There are raised annular and superficial atrophic areas of anesthesia with hyperpigmented borders and hyperesthesia beyond the border, especially on the lower extremities. However, for the past few days the anesthesia has not been present to any extent.

Other features are an edematous right knee, hypersensitivity of the dorsa of both feet, diminished patellar reflexes, a bilateral Babinski sign, some varicosity of both lower limbs, but no edema, and palpable inguinal lymph nodes, which are not painful.

The Kahn reaction was negative. The nasal smear yielded no organisms. On examination no fungi were found.

The histologic examination of a section removed showed a diffuse inflammatory infiltrate but nothing typical.

DISCUSSION

DR MICHAEL H EBERT I made only a cursory examination, and at the time I was not aware of the long duration of the disease. That changes somewhat my ideas about the case. I did test these partly pigmented areas. The woman is a deaf-mute, but she responds to pain by flexing the muscles. The lesions on the leg and the thigh I thought were pretty definite. There seems to be anesthesia in the border. She did appear to have some atrophy of the interosseous muscles of the left hand. I was unable to palpate an enlarged ulnar nerve on either side. I think that the possibility of leprosy is still present. I doubt that one can accept entirely the statement of the patient's relatives that this disease is of so long a duration. I think that further investigation might include a sternal puncture. Dr Otsuki and I had rather striking results in a case of maculopapular leprosy presented to this society by finding organisms in the material obtained by sternal puncture. I think that another biopsy specimen should be taken from the margin of these lesions and a careful study made for Hansen's bacillus. I do not think that one can make an absolute diagnosis.

DR EDWARD A OLIVER There has been a fair number of cases of this disease at one time or another in the Cook County Hospital. It requires much searching to find the organism in some cases. I believe that repeated search should be made for the organism. I also felt a nodule in the lobe of the ear. I believe that it would be wise to excise that nodule and submit it for histologic examination, because often the organisms are found on microscopic examination of the tissue.

DR CLEVELAND J WHITE When we first saw the patient, there was definite anesthesia Atrophy and hyperesthesia were also present When the smear yielded no organisms, I was not sure of the diagnosis Dr Ebert's suggestion of a sternal puncture will be followed We will excise the nodule in the lobe of the ear, as suggested by Dr Oliver

**Pellagra** Presented by DR THEODORE CORNBLEET, DR D COHEN (by invitation) and DR M S KAGEN

Z P, a Negro woman aged 34, has had diarrhea with abdominal cramps intermittently since 1939 She now has a liquid stool and has lost about 30 pounds (13 Kg) in weight A rectal examination revealed a stricture at 3 cm During the past two months a discoloration on the dorsa of the hands and the feet has appeared

The blood cell count revealed a hemoglobin content of 16 per cent, erythrocytes, 920,000, and a differential count of 65 per cent neutrophils, 25 per cent lymphocytes and 10 per cent monocytes The urine was normal, and the Frei test elicited a negative reaction

#### DISCUSSION

DR THEODORE CORNBLEET I believe that this dermatitis is not occasioned by lack of proper food but by what happens to the food after it is ingested She has had vomiting and diarrhea for a relatively long time, and that probably is the basis of her trouble A gastrointestinal disturbance would seem to explain the patient's symptoms

**A Case for Diagnosis** Presented by DR D OMENS, DR H OMENS and DR M S KAGEN

R S, a single Negro woman aged 42, noticed a redness on her legs and thighs three months ago One month ago, she took Lydia M Pinkham's tonic, after which a generalized eruption appeared on the body and the upper extremities

The urine was normal The blood cell count showed a hemoglobin content of 47 per cent, erythrocytes, 2,930,000, and leukocytes, 7,900 The Kahn reaction of the blood was negative

A microscopic study of a section taken from one of the lesions revealed an irregular parakeratosis with no stratum granulosum, a clubbing of the papillary bodies, with thinning of the suprapapillary plates, and, in the corium, a mild perivascular infiltrate composed of lymphocytes

#### DISCUSSION

DR CLARK W FINNERUD The section was a beautiful picture of psoriasis histologically After seeing the section I feel justified in considering the eruption as possibly or probably psoriasis

DR STEPHEN ROTHMAN The patient had definite granular lesions

DR DAVID V OMENS I admit that the section showed typical psoriasis, but the clinical picture suggested that there was something else superimposed on the psoriatic lesion That is why we presented her

**A Case for Diagnosis (Dermatomyositis?)** Presented by DR THEODORF CORNBLEET, DR HERBERT RATTNER and DR M S KAGEN

M N, a married white woman aged 51, had a redness on the dorsa of the hands and on the ears and face three months ago Within a few weeks pains and weakness appeared in the arms and the legs Swelling of the eyelids and feet has been present for the past two months

The patient showed improvement while she was receiving penicillin intramuscularly The edema of the eyelids decreased 50 per cent during the past week, while she was receiving 1,000,000 units of penicillin

The Kahn reaction of the blood was negative. The blood cell count revealed a hemoglobin content of 90 per cent and 6,150 leukocytes, with a differential count of 50 per cent neutrophils, 33 per cent lymphocytes, 10 per cent monocytes, 1 per cent basophils and 6 per cent eosinophils. A roentgenogram showed that the chest was normal. The proctoscopic examination revealed the presence of hemorrhoids. The chemical examination of the blood showed 31 mg of nonprotein nitrogen per hundred cubic centimeters of blood. The sedimentation rate was found to be somewhat increased—18 mm in seventy minutes. The urine was entirely normal. A twenty-four hour urinary creatine determination has not yet been satisfactory.

## DISCUSSION

DR DAVID V OMENS. The histologic picture of the section from the muscle does not show anything definite. The reason is that the section was taken from the distal portion of the extremity instead of the proximal portion. Perhaps if the biopsy specimen were taken from the proximal group of muscles one would get a more definite histologic picture.

DR THEODORE CORNBLEET. It was intended that the biopsy specimen be taken from the pectoral muscle, but through error it was taken from the gastrocnemius muscle. The sedimentation rate, according to the laboratory report, was definitely speeded up. In the differential diagnosis between lupus erythematosus disseminatus and dermatomyositis, the findings speak in favor of dermatomyositis. We had ordered a creatinine estimation made, but the result is not available.

### Tuberculosis Cutis Orificialis with Underlying Pulmonary Tuberculosis

Presented by DR D V OMENS, DR H OMENS and DR M OTSUKA

R J, a white man aged 41, noticed extreme weakness, anorexia and an intermittent cough for the past six months. About four months ago he noticed on the lower lip a crusted lesion, which has steadily increased in size and is now ulcerated. He stated that the lesion is not extremely painful. He also had diarrhea for two weeks before admission to the hospital. The patient has been a chronic drinker.

The essential physical findings are a slightly infiltrated, nickel-sized, crusted, superficial ulcer on the medial portion of the left side of the lower lip, extending to the vermilion border and down over to the mucous membrane of the inner side of the lower lip. Both submaxillary glands are moderately enlarged and somewhat painful. There are crepitant rales in both apexes of the chest.

The sputum yielded tubercle bacilli. The blood cell count revealed a hemoglobin content of 86 per cent, 5,620,000 erythrocytes and 7,150 leukocytes, with a differential count which was within normal range. The Wassermann and Kahn reactions of the blood were negative. The urine contained albumin 1 plus. A roentgenogram of the chest revealed bilateral active pulmonary tuberculosis.

## DISCUSSION

DR H E MICHELSON, Minneapolis. I think that tuberculosis occurring on the mucous membrane of the mouth is comparatively rare. I used to think it a terminal sign, but experts tell me that they see ulceration in the mouth rather often in patients who become reasonably well and they even see cures of the ulcer. It is important to ascertain definitely the state of the pulmonary lesion before making a prognosis.

DR STEPHEN ROTHMAN. I should like to suggest that a smear of material be taken from the ulcer. In this kind of lesion one usually finds masses of tubercle bacilli.

DR DAVID V OMENS. I saw this patient two weeks ago for the first time. At that time he presented a superficial ulcer on the lower lip below the vermilion border, with an extension of the lesion on the vermilion border. When I saw it today for the second time I was surprised to see such a rapid progress in so short a time. I should not be surprised if this is a malignant type of tuberculosis with a rapidly fatal termination.

**Kerions** Presented by DR H E MICHELSON, Minneapolis, and DR CARL W LAYMON, Minneapolis

The patients we see who have kerions are almost always farmers or their children. *Trichophyton gypseum* has been the causative fungus in our cases. One patient has been treated with 20 per cent salicylic acid in petrolatum. One patient with superficial ringworm of the neck also had kerion of the scalp. We have not used epilating doses of roentgen rays in treating kerion. A histopathologic section taken from a third patient revealed epithelioma, so diagnosed by a general pathologist.

#### DISCUSSION

DR H E MICHELSON, Minneapolis: I want to say a word about the sections that were presented. Dr Winer asked a hospital pathologist to make a diagnosis, and he promptly diagnosed epithelioma. One should call attention to the fact that kerionic inflammation causes epithelial hyperplasia.

### SAN FRANCISCO DERMATOLOGICAL SOCIETY

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*April 20, 1945*

**Relapse Following Penicillin Therapy of Early Syphilis** Presented by DR WILLARD M. MEININGER

G. M., a 20 year old single Negro, had positive results of dark field examination, a positive serologic reaction and a genital primary syphilitic lesion in November 1944. His cerebrospinal fluid was normal. He entered Stanford University Hospital on November 15, and his chancre promptly healed with the administration of 1,200,000 units of penicillin given intramuscularly in doses of 80,000 units at six hour intervals. The prepenicillin Kolmer quantitative titer of the blood was 8 units, and the titer remained at that level through Jan. 5, 1945.

He returned for a routine check-up on January 23, with a monorecurrence in which *Treponema pallidum* was demonstrated. His serologic titer had risen to 32 units. The cerebrospinal fluid was still normal. He then received 40,000 units of penicillin intramuscularly every three hours for sixty doses, totaling 2,400,000 units.

The chancre healed, but on February 16 there were three small round erosions in the coronal sulcus. Repeated dark field examinations failed to reveal spirochetes. The erosions appeared herpetic and healed with local application of zinc peroxide medicinal. The serologic titer rose to 64 units but by March 21 had again fallen to 16 units.

The site of the chancre again became ulcerative, and spirochetes were observed on dark field examination on April 6. He was given 0.06 Gm. of oxyphenarsine hydrochloride, and the lesion healed four days later, but some induration persists.

#### DISCUSSION

DR REES B. REES: I should like to ask Dr. Meininger what is his plan for treatment.

DR WILLARD M. MEININGER: Routine therapy consists of a total of thirty weekly injections of oxyphenarsine hydrochloride plus sixty injections of a bismuth preparation, and this system will be followed, provided he does well. This evening there is much induration in the lesion, and I am not sure that this will prove to be the answer. More intensive therapy may be necessary.

DR JOHN M. GRAVES: I should like to ask about the dosage of penicillin and whether you would still continue with it.

DR WILLARD M MEININGER Yes, penicillin is still being used At present a course of 2,400,000 units is administered over a period of seven and a half days It is given intramuscularly at three hour intervals

DR MERLIN T R MAYNARD, San Jose, Calif In one of the recent issues of *The Journal of the American Medical Association* the use of penicillin along with oxophenarsine hydrochloride has been discussed Through the use of the two drugs together, the dose of penicillin could be reduced to approximately one-half and the same percentage of results obtained

I consider that this man has been inadequately treated with penicillin or inadequately treated with oxophenarsine hydrochloride because of the presence of a recurrent lesion I think that, instead, he should have received routine anti-syphilitic therapy with oxophenarsine hydrochloride and an intensive course of penicillin and should not have had the dose of penicillin cut in half A case of this sort should be handled with persistence Once penicillin has been given and failed, the case should not be put in discard, but treatment should be given again to see whether a combination of penicillin and oxophenarsine hydrochloride would effect a cure On the other hand, treatment with penicillin should be followed by routine antisyphilitic therapy until the patients have negative reactions to the tests, otherwise there will be some recurrences

DR ERVIN EPSTEIN I should like to mention the case of a man who had a relapse of secondary syphilis after two years of treatment with oxophenarsine hydrochloride and a bismuth preparation A course of 2,400,000 units of penicillin was given, followed by a second course of 4,000,000 units, or a total of 6,400,000 units, without any effect on the eruption

DR JOHN M GRAVES I do not know whether this case is a good one in which to continue treatment with penicillin, as far as learning anything is concerned Even if one would combine treatments and treat successfully, one would not learn much A fresh case in which there had been no previous treatment would teach more about various combinations and their relationships I understand that at the present time the method used is as follows The patient is treated for ten days, during which time he receives 300 mg of oxophenarsine hydrochloride and 1,200,000 units of penicillin and three injections of bismuth subsalicylate To the group of patients who were mentioned recently in *The Journal of the American Medical Association*, a combination of penicillin and oxophenarsine hydrochloride was given, and it was merely stated that results were better in that group However, nothing was said about the time of observation

DR NORMAN N EPSTEIN This patient has become resistant to penicillin It does not follow, however, that he will become resistant to arsenic when given routine antisyphilitic treatment Because he has relapsed, I think that the course of treatment to be followed should be more intensive than that which Dr Meininger had proposed Injections of oxophenarsine hydrochloride should be given twice a week for ten weeks for a course of twenty injections, and during a certain portion of the time there should be overlapping with injections of a bismuth preparation I should like to recommend that such courses of oxophenarsine hydrochloride be alternated with courses of a bismuth preparation for a period of one year or more The courses of bismuth therapy should not exceed six weeks and should overlap the last four injections of the arsenical

DR GEORGE V KULCHAR Two million units of penicillin is an adequate dose, the tendency is to increase the dose to 3,000,000 units I think that there are going to be even more relapses as time goes on Perhaps the dose should be increased to 4,000,000 units At the present time the treatment being given is 600,000 units of penicillin and five injections of oxophenarsine hydrochloride and five injections of bismuth subsalicylate given over an eight day period

**Chronic Coccogenous Sycosis Treated Locally with Penicillin** Presented by DR HARRY E ALDERSON

S A, a white man aged 31, a sheet metal worker, has sycosis limited to the upper lip and the chin It is contained within well defined borders and presents

an underlying chronic eczematoid eruption. Its duration is over a year. He had been given every kind of treatment (internal and external) mentioned in textbooks, including sulfonamide compounds, and had been the rounds of dermatologists here. In his work he is exposed to various irritating substances, and for protection he wears a gauze mask, which seems to serve as an incubator favoring the growth of organisms. Also, he has had psoriasis, which may account for the type of reaction that his skin presents. His general health and habits are good. His diet is adequate, and he takes good care of himself, although he works extremely hard.

Over a period of several months he received ultraviolet ray treatments, compresses of solution of aluminum acetate, boric acid compresses, local applications of microform crystals of sulfathiazole, cleansing with sulfonated oil and applications of various salves and pastes. Also, the patient remained away from his work for some days. His condition improved at times and grew worse at others. No treatment had any more than temporary effect, so, finally, on the suggestion of Dr Paul Fasal, who saw the patient for me a few times, it was decided to try penicillin locally. Continuous compresses of a solution containing 250 units to the cubic centimeter were applied for a week. Within two days a remarkable improvement occurred. All the follicular pustules and crusting disappeared completely. About two weeks later small local recurrences appeared on each side of the chin in well circumscribed areas. The continuous use of compresses of penicillin was resumed, with prompt relief in two days. One week later there was a slight recurrence in the two small areas on the chin. Application of penicillin salve was started yesterday (250 units to 1 cc).

#### DISCUSSION

DR HARRY E. ALDERSON: Most of the members have seen this patient. I think that I tried about everything that was ever suggested for this disease. The improvement after the continuous application of compresses with penicillin for one week was almost dramatic—all pustules disappeared. There was a slight relapse at two points on the chin, but they were overcome by penicillin compresses. One week later there was a slight recurrence on one side, I started using penicillin ointment, and tonight everything looked fine. When I first saw him he had a confluent pustular eruption involving the entire upper lip and the chin.

DR GEORGE V. KUICHA: I think that penicillin ointment should be used instead of compresses.

DR ERVIN EPSTEIN: I have treated 10 or 12 patients with injections of penicillin, and 75 per cent of them showed decided improvement. In every case, however, there was a relapse as soon as the therapy was discontinued.

#### **Hodgkin's Disease Complicated by a Squamous Cell Epithelioma of the Neck** Presented by DR FRANCES A. TORREY

W. B. H., a white man, was treated in the Dermatologic Clinic of the University of California from May until September 1935 for a seborrheic dermatitis involving the scalp, the face and the body. At that time the eruption was said to have been present for twelve years and to have had a variety of treatments by a number of dermatologists.

On March 13, 1945, he was referred to the Visible Tumor Clinic of the University of California by Dr. Oaks, whom he had consulted on March 5, because of an ulceration on the back of his neck. The lesion had been present about four months and was 2.5 cm. in diameter. Dr. Oaks excised the ulcer and a wide margin of skin and removed the underlying cervical nodes. The histopathologic structure of the ulcer was that of a squamous cell epithelioma.

There was no evidence of metastases of the epithelioma into the cervical nodes. However, the nodes examined were diagnosed as Hodgkin's disease. At this time there was generalized adenopathy, with large firm glands palpable in both axillae. A biopsy of one of those confirmed the diagnosis of Hodgkin's disease.

A biopsy specimen taken on April 4 from one of the chronic cutaneous lesions on the back showed only chronic inflammation

There is also a massive formation of verrucae accuminatae over the entire genitalia and in the anal area Verrucae are also present on the dorsa of the hands and arms

An examination of the blood on April 12, 1945, showed hemoglobin, 88 per cent, erythrocytes, 4,400,000, leukocytes, 22,250, with 60 per cent filamented cells, 29 per cent nonfilamented cells, 4 per cent eosinophils, 2 per cent small lymphocytes and 5 per cent monocytes The Kahn reaction of the blood was negative

#### DISCUSSION

DR. GEORGE V. KULCHAR I think that these lesions on the chin are seborrheic dermatitis The lesions on the trunk look more like parapsoriasis, more like primitive lesions of mycosis fungoides There is definite infiltration Since there is no doubt about Hodgkin's disease of the lymph nodes, it may be a combination of mycosis fungoides and Hodgkin's disease, a transitional form I should like to know what the primary lesions looked like before they were treated at the University of California

DR. FRANCES A. TORREY This patient was seen first in 1934 and at intervals for a year, and then he disappeared When he came back in April 1945, the plaques on his back were suggestive of mycosis fungoides A biopsy specimen was taken from a typical lesion on his back The histopathologic examination showed only chronic inflammation A previous biopsy specimen taken from an axillary node was definitely characteristic of the lymphoblastoma group His white blood cell count showed from 22,000 to 29,000 leukocytes

DR. HARRY E. ALDERSON In addition, I think that he has condyloma accuminata I wonder whether any one has had any experience with resin of podophyllum, as has been mentioned recently in the literature I tried it once in a 25 per cent suspension in liquid petrolatum, and a violent reaction resulted which necessitated almost daily calls on the suffering patient When healing finally resulted, there were no more condylomas

DR. FRANCES A. TORREY Members of the gynecologic department of the University of California have been using it

DR. HARRY E. ALDERSON This man rubbed the preparation in vigorously, contrary to instructions, covering the entire perianal area

DR. MERLIN T. R. MAYNARD, San Jose, Calif I have had 2 patients whom I treated with resin of podophyllum, and they did not complain of any irritation However, the drug did not seem to do anything at all

DR. WILLARD M. MEININGER I have treated 2 patients with 25 per cent resin of podophyllum in liquid petrolatum, and both were cured The one patient had tumorous venereal warts, and a liberal application of the drug caused severe dermatitis venenata The medicine was applied only to tops of the condylomas of the other patient, little irritation resulted, and the lesions disappeared

#### Idiopathic Multiple Pigmented Sarcoma of Kaposi Presented by DR. HIRAM E. MUIR and DR. REES B. REES

P. L., an 84 year old Jewish man, was first seen on Feb. 27, 1945, with regard to the multiple light reddish brown plaques, from the size of a pea to that of a lima bean, on his soles and insteps, which he had first noticed ten days previously A biopsy specimen was taken from his left instep The histopathologic picture included a dilatation of the capillaries, collections of lymphocytoid cells and deposits of hemosiderin pigment in the corium Unfiltered roentgen rays (250 r) were given to each instep, on March 2 and March 27, 1945 The histologic section is presented

## DISCUSSION

DR NORMAN N EPSTEIN I think that this is a characteristic case

DR MERLIN T R MAYNARD, San Jose, Calif The patient also has leukoplakia of the tongue

DR REES B REES I might say that the lesions are fading in color and are less papular since the patient was first seen, which is no doubt due to roentgen ray therapy

**Lichenoid Dermatitis (New Guinea Type)** Presented by DR HARRY E ALDERSON and (by invitation) DR KEMP H DOWDY

For some time in the Dermatological Service of the United States Marine Hospital, San Francisco, there has been an ever increasing number of cases of lichenoid dermatitis, the patients being predominately merchant seamen and Coast Guard personnel returning from duty in the South Pacific Area The following 2 cases are typical

CASE 1—F S, a 50 year old white merchant seaman, reported to the United States Marine Hospital, San Francisco, on April 5, 1945, complaining of severe itching of the arms and the legs

He had been well all his life, and the past thirty-three years he had spent at sea, during which time he had been in practically all the major ports of the world and had no history of cutaneous infection prior to this episode

On Jan 29, 1945, while in port on the north coast of Australia, he began to have swelling, itching and pain in the region of the right ankle The following day he noticed a pustular eruption of the right ankle and leg On January 31, he was taken to a nearby United States Army hospital and given care He returned to the ship the same day, after which time local warm moist applications were applied The cutaneous infection improved

On February 10, he began to notice generalized itching of the trunk, the extremities, the face and the neck Within a few days he noticed peculiar flat-topped lesions over the whole body On February 25, approximately fifteen days later, he was hospitalized at an Army base hospital in Hollandia, New Guinea, where he remained until March 31, during which time the following diagnoses were made by Army dermatologists (1) acute exfoliative dermatitis of the arms and the legs, cause undetermined, and (2) severe atypical lichen planus of the forehead, eyelids, mouth, trunk and extremities

Various local applications were made, with gradual improvement Thereafter he was released to his ship, and on April 2 he was taken ashore to an Army evacuation hospital in Leyte On April 4, he was discharged and evacuated to San Francisco by air

He has had the usual childhood diseases but no severe illnesses in adult life He was hospitalized in San Francisco in 1932, 1935, 1936 and 1939 for various minor illnesses On each admission the serologic reactions of the blood for syphilis were positive After his initial admission in 1932, he received eight injections into the arm and ten into the hip, after a diagnosis of latent syphilis had been made On each admission he was advised to have further treatment, but he did not do so

Scattered over the trunk, face, neck and extremities were many elevated, flat-topped lesions, 2 to 4 mm in diameter, with a livid purple color and with intermingling areas of depigmentation A few superficial pustular lesions were noted on the lower extremities There was generalized lichenification of the forearms and legs, which appeared secondary to scratching The tongue was characterized by gray plaque-like papules, which were well defined Similar lesions were noted on the buccal mucosa The oral lesions were typical of lichen planus

The arms, both the flexor and the extensor surfaces, showed many circular, elevated, flat-topped papules, 2 to 4 mm in diameter, pigmented and having a tendency to coalesce. There was no evidence of exfoliation. Similar lesions were noted on the lower extremities.

The general physical examination revealed essentially normal conditions, except for the cutaneous involvement.

Laboratory findings were as follows. On admission the examination of the urine showed no albumin, sugar, casts or red blood cells. The hemoglobin content was 13.7 Gm. There were 4,500,000 erythrocytes and 15,800 leukocytes, with a differential count of 74 per cent neutrophils, 22 per cent lymphocytes and 4 per cent eosinophils. The Wassermann reaction of the blood was negative and the Kahn reaction doubtful.

Treatment has consisted of daily applications of White's crude coal tar, ultra-violet irradiation, bismuth sodium tartrate twice a week and a high carbohydrate, high protein and high vitamin diet.

Approximately 40 per cent improvement has been noted since the patient's admission on April 5, 1945. The pruritus has ceased.

Microscopically, the specimens submitted consisted of two small elliptic sections of skin, the larger measuring 6 mm in length and up to 2 mm in thickness. There was moderate hyperkeratosis as well as an increase in the stratum granulosum of the epidermis. The rete pegs were focally atrophic and had a "saw tooth" appearance. The basal layer showed slight to moderate degeneration and atrophy. The superficial corium and papillae showed slight focal lymphocytic infiltration. There were a few scattered macrophages filled with coarsely granular, golden brown to brown pigment. The findings were consistent with a diagnosis of lichen planus.

CASE 2—J. T., a 53 year old merchant seaman, reported to the United States Marine Hospital, San Francisco, on Feb. 1, 1945, complaining of severe generalized itching and painful lesions in the mouth. He was admitted to the Dermatological Service and gave the following history.

About Nov. 12, 1944, while aboard ship, on the way to Brisbane, Australia, he noted "cold sores" on the lower lip, which spread to the corners of the mouth and over the tongue and the buccal mucosa. Within a few days itching of the extremities developed, and many small circular raised erythematous areas gradually extended over the face, neck, scalp, trunk and glans penis. The symptoms steadily increased, and the patient was admitted to the United States Army General Hospital, Hollandia, on December 19. A physical examination was made on admission, and the following findings were abstracted from the clinical record.

The entire integument was involved. On the forearms and legs the skin was thickened, dry, red and scaling. On the trunk there were large areas of scaling. The lower lip was slightly denuded and purplish, and on the buccal mucosa there were whitish papules and on the tongue areas where the papillae were gone. There was soft edema of the ankles and of the dorsa of the feet. The patient was thought to have lichen planus.

The treatment consisted of moist compresses of penicillin and supportive treatment. He remained in the hospital at Hollandia until Jan. 11, 1945, at which time he was dismissed and reported to the Marine Hospital February 1.

On admission he was better, but severe pruritus was present. He gave a past history of malaria in 1916 and yellow fever in 1909. He said that he had never had syphilis.

A physical examination in the Marine Hospital revealed the following picture. There was a generalized eruption of flat-topped, annular papules, 2 to 4 mm in diameter, violaceous with fine, white, loosely attached scales, removal of which produced no bleeding. There was decided thickening of the skin of the extremities. The nails of the fingers and the toes showed pitting in the distal portion.

An examination of the blood showed hemoglobin, 14.8 Gm., erythrocytes, 5,200,000 and leukocytes, 9,500, with a differential count of 76 per cent neutrophils,

31 per cent lymphocytes and 2 per cent eosinophils. The urine was essentially normal. The Kahn and Wassermann reactions of the blood were negative. A microscopic examination of scales from various areas showed no fungus.

The treatment in the Marine Hospital has been supportive, with a high vitamin, high protein and high carbohydrate diet, crude coal tar and ultraviolet irradiation and bismuth sodium tartrate twice weekly. The patient has shown gradual improvement. At present there are no active lesions, and the pigmentation is slowly subsiding. The pruritus has ceased.

#### DISCUSSION

DR GEORGE V KULCHAR. I should not think that this is confined to the New Guinea Area only, as last January I saw 2 patients with this disease who returned from the Italian front.

DR HARRY E ALDERSON. There has been a number of such cases in the Marine Hospital, and in some of them the disease was at an earlier stage than that of the case presented to this society tonight. All the patients have typical lichen planus lesions, including involvement of the buccal mucosa. They respond readily to the usual therapy and improve more rapidly in the cooler climate. Many of the lesions are secondarily infected by scratching. One peculiarity is that the face is often much involved. As the lesions subside they leave deeply pigmented macules.

#### Syphilitic Keratosis. Presented by DR WILLARD M MEININGER

W E., a white man aged 50, was first seen on March 14, 1945, with the complaint of inability to work as a presser because of "crusts" on his feet. The rash began on his hands about two years ago, and during the past year it appeared on the arms, legs and feet. Two months of treatment for psoriasis failed to improve it.

He last had gonorrhea in 1926 and has no urethritis or arthralgia. No history of primary or secondary syphilis was obtained. A perianal fistula has been present since 1932, and he was first aware of "lumps" in the perianal region in 1938.

The lesions on the extremities are psoriasiform. There are pitting of the nails and onychiauxis of the thumbs and the toes. Hyperkeratoses are present on the palms and soles, with a verrucous element on the sides of the feet. Smooth lobulated tumors are clustered about the anus. There is considerable induration of a large portion of the buttocks. Pus may be expressed from several sinuses, and some areas are verrucous. The pupils are unequal, deep reflexes are hyperactive, and the patient is somewhat euphoric.

The Wassermann reaction was strongly positive. The spinal fluid has not been examined. The heart and the aorta were normal on fluoroscopic examination. No malignant growth was demonstrated in a biopsy specimen taken from the buttock.

Four injections of iodobismutol with benzocaine have resulted in definite improvement.

#### DISCUSSION

DR GEORGE V KULCHAR. I should like to know about the perianal nodes. I suppose that granuloma inguinale can be considered.

DR NORMAN N EPSTEIN. I thought that he had evidence of psoriasis, although the lesions around the rectum suggested syphilis. Elephantiasis about the anus is suggested as a possibility, or granuloma inguinale. I think that a careful examination of the rectal canal should be made in order to find out whether there is a connection between the mass on the skin and the mucous membrane. Further studies should be made, such as a biopsy, a search for leishmania bodies and a Frei test.

DR OTTO E L SCHMIDT. I saw this patient with Dr Meininger before treatment, and there is no question but that he has improved since I last saw him. I understand that he had only antisiphilitic treatment. I have never seen anything like that before. Older books and pictures describe exactly the same thing that

this man has on his feet With regard to granuloma inguinale, this should not be seriously considered The patient is a white man, which would make it a remote possibility Furthermore, the fact that the lesions on his feet and buttocks have been disappearing indicates that the patient's condition may be due only to syphilis

DR GEORGE V KULCHAR The lesions on his elbows have been present for two years and are typical of psoriasis As for granuloma inguinale, his being a white man does not speak against it, since it does occur in white men

DR NORMAN N EPSTEIN Has a proctoscopic examination been made?

DR WILLARD MEININGER No

DR C W McNITT (by invitation) Was there any evidence of stricture?

DR WILLARD MEININGER The anus admits the finger tip, and the anal sphincter feels like a fibrous ring I am not at all sure that one diagnosis explains the entire picture It seems apparent that syphilis has something to do with the condition of the patient, as he has improved a great deal these past three weeks with bismuth therapy This story of the fistula's being present for a period of twelve years, together with the fact that he has deep abscess formation about the rectum with sinuses from which pus can still be expressed, indicates that there is some pyogenic infection as well Elephantiasis has been described in association with syphilitic keratosis There have been only a few recorded cases of this condition, none as extensive as this

#### A Case for Diagnosis (Monocytic Leukemia?) Presented by DR NORMAN N EPSTEIN

R B, a white married man aged 48, first began to suffer from a generalized eruption about eight months ago This has progressed, and pruritus has been intense up to the present time An examination revealed a generalized eruption involving the entire skin The skin is diffusely reddened and thickened without exudation There is generalized adenopathy of moderate degree, but the inguinal and femoral nodes are large and soft These nodes form a mass the size of a large lemon The oral mucous membranes are not affected

A general physical examination revealed no abnormalities except a barely palpable spleen The laboratory examinations (a roentgenogram of the gastrointestinal tract, a urinalysis and a Wassermann test of the blood) gave essentially normal results The blood count showed hemoglobin, 80 per cent, red blood cells, 3,980,000, and white blood cells, 90,000, with a differential count of 5 per cent polymorphonuclear neutrophils, 9 per cent lymphocytes, 74 per cent mononuclears, 1 per cent eosinophils, 1 per cent myelocytes and 10 per cent monoblasts

A histopathologic examination showed the epidermis to be essentially normal Between the rete pegs and extending into the corium were small masses of cells which appeared to be of the mononuclear type Giemsa's stain confirmed this, many were histiocytes They were larger than lymphocytes

#### DISCUSSION

DR GEORGE V KULCHAR I should like to ask about the original picture and what the skin looked like Has there been any change at all?

DR NORMAN N EPSTEIN The eruption has not changed for several months

DR ERVIN EPSTEIN I think that the clinical picture is a little unusual for monocytic leukemia The characteristic lesions are papules, plaques and ulcers Some feel that monocytic leukemia is a form of myelogenous leukemia Even if this is considered as myelogenous leukemia, the lesions are unusual

DR JOHN M GRAVES I have seen only 1 case of monocytic leukemia with cutaneous lesions The man has ulcers on the lower parts of his legs

DR ERVIN EPSTEIN I have seen ulcerations in 2 cases of monocytic leukemia The ulcers were large, almost gangrenous in type The eruption in this patient is not an exfoliative erythroderma, but it tends more toward this form than

toward the other types of lesions that I have mentioned. It is an unusual lesion for either myelogenous leukemia or monocytic leukemia.

DR REES B REES: I think that the nodule in his right breast is of interest.

DR NORMAN EPSTEIN: Of course, the problem in this case is whether the cutaneous lesions are specific, whether the eruption is leukemic infiltration in the skin or whether it is nonspecific, as seen in other leukemias and other types of lymphoblastoma. I thought that the slide indicated probably monocytic infiltration in the skin, although the amount of infiltration was not great. Most of the cells were mononuclear. Further studies should be made by hematologists. I think that the ulcerations on the patient's legs are compatible with monocytic leukemia. The rest may be or may not be nonspecific generalized dermatitis. Probably, the nodes in the groins are part of this leukemia, in spite of the fact that the rest of the nodes are not very large.

This case was referred to Dr Ernest Falconer, who reported the following observations. After a study of the peripheral blood and bone marrow, it was thought that the disease is not monocytic leukemia but typical of lymphatic leukemia.

**Unilateral Ulceration of the Mouth (Tuberculosis Orificialis?), Probably with Miliary and Ileocecal Involvement** Presented by DR OTTO E L SCHMIDT

A B, a white housewife aged 28, entered the medical ward of Stanford University Hospital April 16, 1945, complaining of abdominal cramps, nausea, vomiting and backache for one year and painful ulceration of the left side of the mouth for three months. The onset of the abdominal symptoms was coincident with pregnancy and continued after the delivery of a normal baby three and a half months ago. There have been intermittent fever and a loss of 14 pounds (6.4 Kg) in weight since January 1945. A painful bleeding eruption of the palate and gums on the left side and the left cheek began in the upper anterior part of the gingival sulcus shortly after parturition and has spread progressively since.

There is a friable granular-nodular confluent ulceration covered with a thin grayish exudate involving the gingivae, buccal mucous membrane, hard and soft palate and faucial pillars only to the left of the midline. Cervical and submaxillary nodes are palpable. There is a mass (kidney?) in the right upper quadrant of the abdomen and an egg-sized mass in the right lower quadrant. A small grayish nodule is seen in the left sclera.

The laboratory examination of the blood showed hemoglobin, 55 per cent, erythrocyte sedimentation rate, 34 mm in one hour, plasma protein, 6.8 Gm per hundred cubic centimeters. Examinations of the urine and the stool were non-contributory. Tuberculin in a 1:1,000 dilution elicited a negative reaction. The acid-fast stains of material from the mouth, the bladder and the cervix revealed no tubercle bacilli. The roentgenograms of the chest showed diffuse nodular infiltration. The barium sulfate enema showed a deformed ileum and cecum. The coccidioidin test revealed no organisms after twenty-four hours.

#### DISCUSSION

DR HARRY E ALDERSON: This seems to me a good example of local inoculation of the mucous membrane with the patient's own sputum.

DR JOHN M GRAVES: Does the patient have pulmonary or laryngeal tuberculosis?

DR OTTO E L SCHMIDT: She has diffuse miliary infiltration throughout both pulmonary fields. The test for acid-fast bacilli has not yet been made, since the patient has been in the hospital for only three days. A tuberculin test elicited a negative reaction. Of course, in miliary tuberculosis there may be a negative reaction to tuberculin.

DR JOHN M GRAVES What sort of lesion would be expected in a case of inoculation tuberculosis in which there had been a negative reaction to the tuberculin test? Would anything like a primary tuberculous complex be obtained?

DR OTTO E L SCHMIDT I cannot answer that, to be absolutely sure. First, the patient has a unilateral distribution, the eruption involving so much of one side only. No sputum was brought up, but she might have vomited tubercle bacilli. It is not the sort of disorder seen ordinarily. Patients whose sputum contains organisms are apt to inoculate the mucous junction.

DR JOHN M GRAVES I had a patient a good many years ago who had tuberculosis of the hard palate. She had a denture that did not fit well. She had definite pulmonary tuberculosis and coughed up sputum, which brought up bacilli that lodged between the palate and the alveolar ridge. The case resembled this one very much.

DR OTTO E L SCHMIDT The possibility of involvement of the maxillary division of the fifth nerve by herpes zoster was also brought up. It is hard to prove now, as she has had the eruption for three months—that is, the lesions have progressed in the past three months.

DR JOHN M GRAVES Should not a biopsy be performed?

DR OTTO E L SCHMIDT This has been proposed. The lesion is certainly typical of tuberculosis of the mucous membrane, and that should be the presumptive diagnosis. The nodules are apparent within the lesions. The patient is obviously gravely ill, which suggests one of the diseases of the tuberculous type, including coccidioidomycosis. The condition should be differentiated from any other disease that might mimic a tuberculous picture. Most likely it is miliary tuberculosis with involvement of the mucous membrane, and one should accept this diagnosis until one can prove it is not.

DR FRANCES M KEDDIE Another possibility occurred to me—that is, histoplasmosis. Pulmonary and oral lesions are not infrequently present at the same time.

DR NORMAN N EPSTEIN Coccidioidomycosis should also be considered.

#### Roentgen Ray Dermatitis Treated with Radon Ointment Presented by DR JOHN L FANNING

P G, a white man aged 27, is the office manager of an electric company.

In January 1943, he examined rocks for over an hour, using a hand fluoroscope and an x-ray machine. The next day he felt a sunburn on the fingers, and in a week severe dermatitis developed on the backs of the fingers and the right hand which was treated until April, when it was healed.

He was next seen in January 1944, with evidence of roentgen ray dermatitis and beginning ulceration of the right third finger. Later ulcerations appeared on the right second and fourth and the left second and fourth fingers. He was treated with a bland ointment, urea and aloe without results. The severe pain necessitated sedation. In May amputation of the right third finger was considered.

The patient was seen in July by Dr Templeton, who suggested radon ointment, 100 electrostatic units and later 200 electrostatic units for eight hours weekly. The right finger was healed in September, and all fingers were healed in April 1945.

New ulcerations and keratoses are developing on the right third finger and more dermatitis on the back of the right hand.

#### DISCUSSION

DR REES B REES If it is at all feasible, plastic reconstruction should be considered and done as soon as possible.

DR HARRY E ALDERSON It would be difficult to reconstruct the dorsa of the hands and fingers. On the other hand, I do not see what else can be done, unless the eruption is controlled with applications of radon.

DR MERLIN T R MAYNARD, San Jose, Calif I have said a number of times before that every patient with radiodermatitis should receive vitamin D for a long time to soften the scar I have seen eruptions like this occurring over and over again I think that the patients should be receiving this form of therapy as a routine There is less contraction as well as less sclerosis, and as far as grafting is concerned, the tissues would be in better condition for it Besides, it keeps an accumulation of calcium from forming in collagenous tissues, which cuts down circulation or devitalizes the areas

DR. JOHN L FANNING, Sacramento, Calif The patient had so much pain with one of his fingers that at one time I thought it should be amputated Dr Templeton saw him and suggested radon ointment The patient began using it, and the ulcer healed completely, which to me is rather remarkable In a short time other areas broke down, and with the application of radon ointment healed in from six weeks to three months

**Dermatitis Venenata Due to a Penicillin-Containing Ointment** (Photograph only, patient not presented) Presented by DR OTTO E L SCHMIDT

R K. C., a 40 year old white man, a hotel clerk, first entered the Stanford University dermatologic clinic complaining of crusted ulcers of the scalp of two months' duration and ulcers of the right thumb and the left shin of two weeks' duration He had used ammoniated mercury ointment, with little effect

Examination showed a malnourished, pale man Scattered over the scalp were crusted, purulent ulcers measuring about 2 cm in diameter A purulent paronychia involved the right thumb On the left midtibial surface was a 6 cm excavated crusted ulcer with peripheral erythema

The Wassermann reaction was negative, and a culture of material from the ulcer on the shin showed a heavy growth of hemolytic streptococci and Staphylococcus aureus, coagulase positive Potassium permanganate compresses and bismuth tribromphenate ointment brought about healing of the lesions on the scalp but did not affect those on the thumb and the shin Penicillin in an ointment (250 units per gram of petrolatum base) was used twice daily, and in ten days the ulcers on the thumb and the leg were two-thirds healed The preparation was changed to one containing penicillin, 500 units per gram of a Lanette wax base Ten days after the change, a confluent erythematous papular eruption appeared around the lesions on the right leg, in the exact area covered by the ointment The plain base has not yet been obtained for patch testing, nor has a solution of penicillin yet been applied

DISCUSSION

DR. OTTO E L SCHMIDT This is an incomplete presentation, since I do not have the results of the tests with all the ingredients of the ointment base I think that this case proves that penicillin is not as innocuous as the first reports indicated

NEW YORK DERMATOLOGICAL SOCIETY

Hans J Schwartz, M D, *President*

George C Andrews, M D, *Secretary*

April 24, 1945

**Erythema Annulare Centrifugum** Presented by DR FRED WISE

J C., a girl aged 2 years and 3 months, has had intermittent eruptions of urticaria papulosa since she was 3 months of age The baby's general health has been excellent, and the eruptions seem to be uninfluenced by dietetic restrictions About two months ago a gyrate eruption appeared on the abdomen and

the thighs; the lesions occurred at irregular intervals, lasting a week to ten days, and faded spontaneously at different intervals

Examination showed widespread, well defined, ringed lesions, varying in diameter from 4 to 8 inches (10 to 20 cm), on the abdomen, buttocks and thighs. The borders were  $\frac{1}{4}$  inch (0.6 cm) broad, bright red, and faintly elevated at their outer edges, while the inner edges sloped toward the interior of the circles, which showed no visible changes. The mother stated that the ringed lesions disappeared promptly after the child had a Schick test.

#### DISCUSSION

DR. V. H. CORNELL (by invitation) I agree with the diagnosis, this is an extensive case.

DR. FRANK C. COMBES. I can confirm the report that these lesions disappear on exposure to ultraviolet radiation from a quartz mercury vapor glow lamp.

#### Junction Nevus. Presented by DR. ANTHONY C. CIPOLLARO

H. W., a girl aged 13, consulted me on April 14, 1945, because of a lesion on the forehead, which has been present since birth. There has been no definite sign of growth, and it has never been treated.

The lesion is the size of a marble, situated in the middle of the forehead near the right eyebrow. It is elevated and light brown and is firm to the touch. The major portion of the lesion extends below the surface of the skin.

The case is presented, first, to determine the type of lesion on clinical grounds, and, second, if treatment is indicated, to ascertain what type of treatment should be instituted.

#### DISCUSSION

DR. FRED WISE. Since there is a hard infiltrated area below the pigmented surface, I should be inclined to regard this as a potentially dangerous lesion. I cannot say whether I should advise removal with wide excision or whether I should leave it alone.

DR. MAURICE J. COSTELLO. I agree with those who think that this lesion should be excised conservatively.

DR. GEORGE C. ANDREWS. In a series of about 200 cases of melanoma it was found that in all cases in which the melanomas had been excised in children under 10 years of age there was 100 per cent cure. This child's age is in favor of this treatment. If the lesion is excised now, her chances are excellent, whereas if melanoma develops later in life her chances will not be so good.

DR. ANTHONY C. CIPOLLARO. I presented this case for the reason brought out in the discussion. The patient's father is a physician, who wanted my advice as to removal of the lesion. I am not sure that I agree with the suggestion that the lesion should be excised not too widely, with a fair margin for diagnostic purposes. If there is any possibility of this being a dangerous lesion, it can be left alone. However, I do not see what harm there is in excising a potentially dangerous lesion. I have seen melanocarcinomas develop in 2 patients several years after the removal of junction nevi.

#### Granuloma Annulare Generalized. Presented by DR. EUGENE E. TRAUB

P. W., an 8 year old boy, first noticed eruptions on both legs after an attack of measles in May 1944. New lesions appeared on the trunk and the upper extremities, and the eruption gradually became generalized. The only drugs that the boy was known to have taken were 6 tablets of a sulfonamide compound in February and November 1944 for a respiratory infection which his mother termed "flu," and a cough medicine on the occasion of measles.

Examination showed a generalized eruption of papular and nodular lesions irregularly scattered over the chest, the back (particularly the interscapular region), the buttocks and the upper and lower extremities.

On the extensor, inner and flexor surfaces of both legs, where the eruption originally had started, are firm plaques up to almost half-dollar size, smooth, elevated and movable with the skin against the underlying structures. These plaques are shiny and violaceous. Some of these plaques are bordered by reddish, closely set nodules, forming a ring around the somewhat depressed center.

The papules on the trunk are discrete and coalescent and vary in size from that of a pea to that of a bean. They are skin colored, many of them with a tendency to form rings. On the buttocks there are elevated pink-reddish wheal-like lesions up to a quarter in size.

The lymph nodes were palpable but not appreciably enlarged, the spleen was not felt.

The urine contained no albumin. Examination of the blood showed red cells, 3,230,000; white cells, 4,850 (borderline leukopenia), hemoglobin, 84 per cent and color index, 1.0. The differential count showed 25 per cent neutrophils, 3 per cent eosinophils, 3 per cent monocytes and 69 per cent lymphocytes. A roentgenologic examination revealed that the chest was essentially normal. An examination of the thorax showed the total heart area relatively a shade small, yet within 10 per cent of normal in size and contour. There was a slight accentuation in both hilar regions. The pulmonary fields were otherwise clear, with no evidence of parenchymatous infiltration or pleural involvement.

The microscopic diagnosis was Spiegler-Fendt sarcoid (?). Further sections showed suggestions of granuloma annulare.

The section showed a relatively normal epidermis. The entire corium was filled with islands as well as with a diffuse cellular infiltration. The majority of these cells were of fixed connective tissue type. In addition, there were rather large cells with deeply stained nuclei. There were some lymphocytes and plasma cells. The connective tissue fibers around the nodules were not broken. There was no pigment in the methylene blue stain.

The deeper sections showed a normal epidermis with a parakeratotic scale. Scattered throughout the corium were islands of round cell exudate consisting of mixed cells.

There was a diffuse cellular exudate which was especially evident in the lower part of the corium and also affected the hypoderm. In the midcorium there was an island of non-nucleated connective tissue fibers, which had lost their normal contour and had become swollen. In the center of this nodule there were some blue-staining granules and remnants of nuclei. The cellular exudate consisted of lymphocytes, connective tissue cells and plasma cells and fragmented nuclei. The blood vessels appeared occluded or with hypertrophied walls.

Old tuberculin (April 20, 1945) in dilutions of 1:1,000,000, 1:100,000 and 1:10,000 elicited negative reactions.

#### DISCUSSION

DR A. BENSON CANNON: This is a generalized eruption, there are no annular lesions and no infiltrated plaques, but the lesions present are red. One should reserve opinion as to the final diagnosis, especially as there is some doubt about the histologic diagnosis. I suspect that eventually this will develop into lymphoblastoma rather than remain in a benign form, such as granuloma annulare or the Spiegler-Fendt sarcoid. It is my impression that the Spiegler-Fendt sarcoid has been described in modern medicine as eventually becoming malignant.

DR FRED WISE: I should not think this a Spiegler-Fendt sarcoid from the little knowledge I have of that disease. It certainly had not the slightest resemblance to the case described by Lewis. I think that this is the disseminated type of papular and discoid form of the disease, which is more common in infants and does not become plaque-like. In infants papular granuloma annulare is seen without circinate lesions. In this patient the lesions are unusual, and I should be interested in hearing about further histologic examinations and staining to get a better idea of the whole picture.

DR PAUL E BECHET While many of the lesions are most atypical, there are a few on the back of the hand which present an annular formation with borders more elevated than the central portion, which is distinctly flatter. The appearance of these particular lesions is sufficiently characteristic for one to make the diagnosis of granuloma annulare.

DR GEORGE M LEWIS In regard to the question brought out by Dr Cannon, I think that Spiegler-Fendt sarcoid is not a good term, as the disease has no relation to the Boeck or the Darrier-Roussy sarcoid. It was thought that the cases could be divided into two types: one, the benign form, in which the disease is localized and the prognosis good for cure, and, the other, the disseminated form, which perhaps might be difficult to distinguish from lymphosarcoma. Certainly, the histologic architecture is distinctive in most cases. It would seem from the literature and from the cases I was able to follow that it is an entity and may be distinguished from other lymphoblastomatous diseases.

DR EUGENE F TRAUB This boy has had two sections removed for microscopic study, the diagnosis is not yet conclusive. But the eruption in this case seems more nearly to conform to generalized granuloma annulare than to anything else, except that there are certain features suggesting lymphoblastoma. The lesions on the leg are certainly peculiarly colored, and the question of Spiegler-Fendt sarcoid was raised because it does actually undergo certain changes similar to lymphoblastoma, and the blood picture is not quite what it should be.

#### **Morphea-Like Epithelioma and Basal Cell Epithelioma of the Face Cured by Roentgen Ray Therapy** Presented by DR MAURICE J COSTELLO

E D, a woman aged 54, a private patient, was seen by me for the first time on May 23, 1944, at which time she had a lesion on the right cheek which had been present four years. It was sharply margined, with a scalloped border inclosing a hard waxlike lesion, with a pearly, shiny, elevated nodular border, involving a half-dollar-sized area, including the right ala nasi, the right cheek and the right side of the upper lip. There was a linear ulceration in the right nasolabial fold. She also had two basal cell epitheliomas, one half the size of a dime and the other the size of a dime, on the left cheek and on the left side of the forehead.

During the period between May 23 and Aug 17, 1944, she received roentgen rays, 4,500 r directed to the lesion on the right cheek, 3,500 r to the lesion on the left cheek and 1,800 r to the lesion on the left side of the forehead.

The patient has hypertension. She states that for some time prior to the development of the epithelioma on the right side of the face she had been treated for nasal polyps, which she says disappeared during treatment for the aforementioned lesion.

The lesion on the right cheek received 4,500 r as follows: 1,500 r unfiltered, 1,450 r filtered through 1 mm of aluminum, 1,050 r filtered through 2 mm of aluminum and 500 r filtered through 3 mm of aluminum.

#### **DISCUSSION**

DR FRFD WISE The result is excellent.

#### **Radiodermatitis** Presented by DR ANTHONY C CIPOLLARO

M S, a woman aged 50, consulted me on March 22, 1945. She stated that ten years previously she had a tumor on the left side of the neck, which was excised and found to be a giant cell tumor. The left side of the chest, including the back and the clavicular area, was irradiated. Two years later there was redness, and during the past six months several ulcerated areas have developed in the scapular and clavicular areas.

The patient now presents a large area of radiodermatitis with a superficial ulcer near the clavicle and several smaller and more superficial ulcerations in the scapular region. These ulcerations may have resulted from trauma and scratching,

because there is considerable pruritus. Overlying the radiodermatitis there is also dermatitis resulting from topical remedies.

This case is presented for discussion as to the best therapeutic procedure. Is this a suitable case for plastic surgical intervention?

#### DISCUSSION

DR EUGENE F TRAUB If only the question of time is involved, why not do a plastic operation now?

DR A BENSON CANNON I saw some photographs by Morginson and the men in St Louis that showed astounding results after penicillin ointment had been used. The photographs showed the conditions before and after treatment, including a case with ulcers, and the subsequent photographs showed a well healed scar. This substance was tried in several cases. One of the advantages was that it was an analgesic and relieved pain immediately.

DR ANTHONY C CIPOLLARO I am glad that the discussion of penicillin ointment came up, because when I first saw the patient I treated the ulcerated areas with penicillin but found that a dermatitis developed around the ulcerations, then I used halibut liver oil ointment. Further dermatitis developed, and I had to stop these treatments. Now she has radiodermatitis and remnants of superficial ulcerations. I agree that the only way to cure this condition permanently is by a plastic operation.

#### Nummular Eczema. Presented by DR ANTHONY C CIPOLLARO

C S, a man aged 52, American born, consulted me on Jan 16, 1945, because of an eruption of five days' duration, which was fairly generalized. He had had a similar eruption about ten years previously. When he was first seen by me, the patient had an exudative vesicular dermatitis in patches and in groups of lesions, affecting most portions of the body. After several weeks of treatment with soothing topical remedies, baths, wet dressings and roentgen rays, the eruption improved greatly. Then new lesions appeared at the margins of the old lesions. These have been for the most part grouped vesicles with severe pruritus, most severe at bedtime. Treatment has been continued with various topical remedies, roentgen rays, nicotinic acid and other drugs, with steady, but extremely slow improvement. It was thought that he might have an aberrant form of dermatitis herpetiformis, and he had laboratory tests carried out with this in view. His basal metabolic rate was normal. His blood count was normal except for 9 per cent eosinophils. An intradermal test with toxoid gave a slight reaction. Results of patch tests with potassium iodide and sodium bromide were negative. A biopsy section showed structure of nummular eczema.

The case is presented for diagnosis and for therapeutic suggestions.

#### DISCUSSION

DR EUGENE F TRAUB I wonder why the Senear-Usher type of pemphigus has been excluded in this case.

DR MAURICE J COSTELLO My clinical impression is that the disease in this case is chronic lichenoid and discoid dermatitis. I thought that this patient was Jewish until it was mentioned that he was not.

DR GEORGE C ANDREWS This man has carious and infected teeth. However, I also got the impression that this might be some erythematous type of pemphigus—the Senear-Usher type. The only objection to this diagnosis is that the vesicular lesions on the palms looked like an "id," and this is not expected in the Senear-Usher type. I think that the man's general condition should be studied, the blood count, the leukocyte count and roentgenograms should be examined for focal infections, and perhaps in that way one may arrive at the causative factors. I do not see how the eruption can be called any more than eczema at present.

DR FRED WISE My impression of this eruption is that it is a good example of exudative discoid dermatosis, described by Sulzberger and Garbe.

DR. FRANK C. COMBES I agree with Drs Costello and Wise I think that this patient would do much better if he got out into the country

DR. ANTHONY C. CIPOLLARO I appreciate the discussion I considered this case one of nummular eczema because all the scientific evidence points to this diagnosis The biopsy indicates that, and there was no evidence of Senear-Usher disease in the biopsy specimen The blood count showed 5,000,000 red blood cells, and the differential count was normal except for the eosinophils, which were 9 per cent I did not study his teeth, but the doctor who examined him said he was all right physically He is definitely psychopathic He had a "nervous breakdown" at 18 and has had trouble with his mother all his life He lives out in the country, has a good business and is financially independent. The "id" eruption on the palms may be explained by the fact that he has dermatophytosis in addition to the eruption for which he was presented

**Radiodermatitis of the Dorsal Surface of the Hands.** Presented by DR. FRED WISE

J. C., a white woman aged 20, was seen at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on April 17, 1945, presenting lesions of eighteen months' duration (two months after exposure to roentgen rays) The patient stated that she had been treated with one exposure to roentgen rays nine minutes long, in September 1943 A week later her hands became edematous, many large bullous lesions developed, which subsequently became infected The infection subsided in two months, after which the lesions broke out on the hands, showing the changes presented today An ulcer developed on the right thumb in February 1945 During the winter the hands are numb and become tender and edematous

On the dorsal surfaces of both hands, well demarcated by sharp straight lines at about the junction of the middle and upper thirds of the hands, are pigmented and depigmented and telangiectatic areas The skin is atrophic and greatly reduced in elasticity There are several irregular raised rough hyperkeratotic growths, from the size of a pinhead to that of a pea A shallow ulcer the size of a small bean, which is irregular, painful and tender, developed on Feb 17, 1945, on the inner surface of the distal phalanx of the right thumb On diascopic pressure some telangiectatic areas fade almost entirely, leaving yellowish spots, but others are not altered

The patient is being referred for plastic repair of the ulceration on the thumb and destruction by electrocoagulation of the hyperkeratotic plugs A salve containing vitamins A and D was prescribed to be used as an emollient application for the hands She was advised to avoid exposing her hands to the sun, to keep them out of dishwater and to prevent contact with irritating soaps and chemicals

The erythrocyte count was 3,750,000, and the leukocyte count was 3,750 per cubic millimeter The hemoglobin was 11.8 Gm per hundred cubic centimeters, or 71 per cent The color index and the differential count were normal

**Tuberculosis of the Skin** Presented by DR. FRED WISE

K. B., a Negro woman aged 34, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on April 10, 1945, presenting lesions of seven months' duration She had had "rheumatism of the hips" at 16 years of age She complains of pain in the chest and shortness of breath on moderate exertion The first pregnancy resulted in a stillbirth at nine months; the second, in a miscarriage at six months, and the third, in a premature baby at seven months, which lived for seven months She was treated for syphilis at the Board of Health, with intravenous and intramuscular injections for one year, from 1938 to 1939 In 1941 she was given twelve more injections into the hip by a private physician, after which she was discharged as cured The last six or seven hematologic tests were said to be negative

The patient presents three ulcerated lesions. The lesion on the middle of the anterior surface of the left arm began in June 1944, the one on the upper part of the inner surface of the left breast, in July, and the one on the base of the left side of the chest, in October. The lesion on the arm is 2.5 by 1.5 cm, ovoid, with an ulceration in the center which is excavated, with a dirty grayish base from which a mucopurulent fluid exudes. There is a satellite pea-sized lesion 3 cm below it. The lesion on the breast is irregular, ulcerated in the center and raised a few millimeters, with many fine clawlike keloidal branchings extending to the periphery. It is tender and infiltrated, the tissues being matted together, but the whole mass moves fairly freely on the subcutaneous structures. The lesion on the base of the left side of the chest, 2 by 0.5 cm in size and 1 cm thick, is placed horizontally. It has a linear ulceration in the center, sloping rounded surfaces and is doughy in consistency.

The Wassermann and the Kahn reactions of the blood were negative, and the urine was normal. The hemogram was normal except for a white cell count of 3,800. A roentgenologic examination of the chest, recently taken at the Board of Health, was said to show osteitis of the ribs.

A histologic section, taken from the lesion of the arm, was examined by Dr. Charles F. Sims, and the eruption was diagnosed as tuberculosis of the skin. It was interpreted as follows:

"The epidermis is decidedly acanthotic in the center of the section. However, at one point it has broken down. The upper, middle and deep parts of the corium present a massive cellular reaction composed of groups of epithelioid cells surrounded in part by a moderate mantle of small round cells. In the area of ulceration many polymorphonuclear cells may be noted. Some scattered giant cells are visible. The vessels throughout are moderately dilated."

#### DISCUSSION

DR. FRANK C. COMBES: I do not think that there is sufficient evidence present to call this tuberculosis. I should want further study done to eliminate the possibilities of its being a gumma. It is unusual for this type of tuberculosis to develop at this patient's age, although tuberculosis is common in those areas. One should be able to find tubercle bacilli in these lesions.

DR. MAURICE J. COSTELLO: I think that occasionally in patients suffering from scrofuloderma lesions like this may be seen, and I should be inclined to agree with the presenting diagnosis for that reason. The lesions arising independent of underlying tuberculous foci may be regarded as tuberculous gummas.

DR. A. BENSON CANNON: I suggest that inasmuch as she is known to have syphilis, even though her Wassermann reaction was negative, this patient be given the benefit of therapy, unless the eruption is proved by inoculation of a guinea pig to be tuberculous. I understand that this has not as yet been done.

DR. FRED WISE: I appreciate the significance of Dr. Cannon's remarks, but I have a section from the lesion on the arm which shows typical tuberculosis, no other diagnosis could possibly be made under the circumstances.

#### A Case for Diagnosis (*Poikiloderma atrophicans vasculare*?) Presented by DR. MAURICE J. COSTELLO

J. G., a man aged 52, from the outpatient department of Lenox Hill Hospital, presents several linear and round areas consisting of radiating telangiectatic vessels. These patches blanch on pressure, and there is a suggestion of atrophy in the center of them. They are located mainly above the waistline, on the right pectoral region, the supraclavicular area and the back.

The patient stated that he has had several epistaxes during the past year.

This eruption began in 1920. He had had streptococcal septicemia in 1933, and, after an operation for submucous resection, has a traumatic perforation of the nasal septum.

The Wassermann reaction was negative, and his gallbladder had been removed some years ago

## DISCUSSION

DR FRED WISE This is a difficult case to diagnose. It does not resemble the classic ones, such as the one I presented. But I understand that the changes in elastic tissue are characteristic, and poikiloderma may sometimes be differentiated on the basis of these changes alone. It would be interesting to get a biopsy specimen from this lesion and to see whether any peculiar changes in the elastic tissue are present.

DR GEORGE C. ANDREWS The man's flushed face, telangiectasis and acneform lesions on the sternal area are characteristic of polycythemia vera, and he said that since last year he has become extremely short of breath.

**Parapsoriasis en Gouttes** Presented by DR FRED WISE

R. R., a man aged 28, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on April 12, 1945, presenting lesions of three months' duration. He gave no history of previous cutaneous disorders. His general health has been unaffected. There are no subjective symptoms.

The lesions first appeared on the waist and the upper extremities and spread on the following day over the entire body. The patches did not undergo involution, nor have they become aggravated. The lesions are generalized, superficial and profuse, covering the entire trunk and extremities, except for the middle and the distal phalanges, the right palm and the soles. The scalp and the face are unaffected except for the eyelids and infraorbital regions.

The lesions vary in color from yellowish red to bright red. They consist of papules from the size of a pinhead to that of a split pea to that of a bean, forming irregular networks enclosing the white irregular areas of the unaffected skin. Some of the lesions are covered with fine, dry, sparse central and peripheral scaling, the latter being most pronounced on the lower limbs. Most of the lesions show delicate parallel lines of the finely wrinkled skin, which are arrayed oblong on the upper extremities and obliquely on the back. The lesions fade partially on diascopic pressure, revealing yellowish patches, some showing fine telangiectatic capillaries. The lesions on the legs are only slightly altered. The left epitrochlear and axillary lymph nodes are enlarged.

The routine laboratory tests revealed no abnormalities. From a section taken from the right thigh the disease was diagnosed by Dr. Charles F. Sims as "possible parapsoriasis." The interpretation is as follows:

"The epidermis is mildly and somewhat irregularly acanthotic. At one or two points slight parakeratosis may be noted, particularly manifest over areas in which an infiltration is present in the corium. The latter may be seen in the papillary and subpapillary zones, as small masses hugging the epidermodermal junction. At these points the basal cell margin is somewhat disorganized, and exocytosis is visible. Histologically, psoriasis can be eliminated."

## DISCUSSION

DR MAURICE J. COSTELLO I saw several small oval atrophic lesions in addition to the others. I suggest the diagnosis of parapsoriasis atrophicans, similar to the disease in the case which I presented to this society several months ago.

**A Case for Diagnosis (Sarcoid? Leprosy?)** Presented by DR A. BENSON CANNON

P. L., a Filipino aged 45, was born in the Philippine Islands. His family history is not remarkable. At 16 years of age he left the Philippine Islands and has lived in the United States ever since; he is a steward.

On arriving in this country he felt a numbness of the left foot and lower part of the leg, which gradually diminished over a period of eight years. During the past ten years, however, he has noticed some numbness of both feet.

In 1939 a dollar-sized lesion developed on the right cheek, which gradually spread to involve the present location. It has been asymptomatic and has diminished in the past two years.

Examination reveals a coppery, slightly indurated eruption with an irregular, clearly demarcated border. Some of the border is slightly elevated. There is no generalized lymphadenopathy. There is definitely diminished sensation to pain, temperature and light touch in both lower extremities, most decided in the toes. The deep and the superficial reflexes are normal. Otherwise, the physical examination shows essentially a normal condition.

Examination of the blood showed hemoglobin, 16.0 Gm, red blood cells, 5,900,000, white blood cells, 9,100, with 56 per cent polymorphonuclear leukocytes, 43 per cent lymphocytes and 1 per cent basophils. The urine was normal. The erythrocyte sedimentation rate was 9 mm per hour.

#### DISCUSSION

DR MAURICE J COSTELLO: From the clinical point of view this patient has leprosy. The lesions are fairly typical, he has in addition to the highly suggestive cutaneous lesions a visibly enlarged great auricular nerve on the right side. I think that the diagnosis will be substantiated by further examinations.

DR FRANK C COMBES: Is this the tuberculoid manifestation of sarcoid?

DR FRED WISE: In this patient a careful search should be made for bacilli, in the skin as well as the nasal mucosa. I have little doubt about this being leprosy of the type first described by J. Jadassohn.

#### **Poikiloderma Vasculare Atrophicans (Jacobi)** Presented by DR. FRED WISE

F. S., a woman aged 27, under the care of Dr. Cole of Cleveland, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on April 13, 1945, presenting lesions of twenty years' duration. There is no history of a similar cutaneous disorder in the immediate family or relatives. She had measles and scarlet fever during childhood. The tonsils were removed when she was 14 years of age. She began to menstruate when she was 11. Menses have been regular and normal since. She is subject to colds and has been having headaches in the region of the right temple for the past two years. Her general health seems to have been unaffected. There are no subjective symptoms.

When the patient was 7, there appeared a round smooth white scaly patch, 2.5 cm in circumference, on the front of the right thigh and similar spots on the anterior surface of the forearms. These never regressed but became larger until she reached the age of 14. They have since assumed the characteristics of the other lesions. When she was 14, she began to avoid being in the sunshine, because she perspired excessively. From 14 to 20 years of age she paid no attention to her skin. At 20 she noticed patches on the outer surfaces and the sides of the thighs, on the buttocks, and in the left axilla. Since then brownish patches have developed on the hypogastric region. For the past two years the brownish patches have been appearing on the abdomen, the chest and the back. The redness on the breasts has also appeared within the past two years.

The patient presents symmetric lesions on the trunk and the extremities. Almost the entire body is involved except for some parts of the upper halves of the breasts and parts of the abdomen, the thighs and the legs. Most of the lesions consist of reddish telangiectatic areas, together with atrophic spots revealing a retiform arrangement and covered in some areas with dry, flakelike scales, loosened at the edges. These lesions are more extensive on the arms, the buttocks and the lower limbs, down to below the knees, being almost confluent in these areas. There are also confluent areas around the neck. The upper part of the back, the breasts and the abdomen are comparatively free of lesions except for irregular hyperpigmented spots varying from the size of a pea to that of a palm. The face is erythematous, and the eyelids are edematous. There are some telangiectatic vessels on the cheeks. The soles are hyperkeratotic, and to a lesser extent so are the

palms The oral mucosa and the nails appear normal There are no enlarged lymph nodes

The routine laboratory tests revealed normal conditions

According to a section taken from the right thigh, the disease was diagnosed by Dr Charles F Sims as poikiloderma The interpretation is as follows

"The epidermis is thinned, with obliteration of the rete pegs and the corresponding papillary bodies Basal cell layer liquefaction may be noted in many parts of the section A mild exocytosis is present In the upper corium is a diffuse cellular reaction composed for the most part of small round cells and an occasional wandering connective tissue cell Parenchymatous edema of the collagen may be noted in the upper corium The vessels of the upper corium are dilated, and some appear telangiectatic Many scattered chromatophores are present

"Weigert's elastic tissue stain shows elastorrhexis in the zone of infiltration Perles' stain is negative for hemosiderin"

#### PHILADELPHIA DERMATOLOGICAL SOCIETY

Carmen C Thomas, M D, *Chairman*

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May 18, 1945

Angioneurotic Edema Presented by DR ISADORE ZUGERMAN

R S, a white man aged 22, presents a palpable thickening of the upper lip extending to the mustache area Erythema is present occasionally One year ago the patient was stationed at a naval base in the Aleutian Islands It was at that time that he first noticed, and was treated for, a persistent swelling of his upper lip, which he said "sticks like needles and draws"

The Wassermann reaction of the blood was negative The urine was normal A complete blood count was within normal limits

#### DISCUSSION

DR HERBERT J SMITH The swelling does not look like angioneurotic edema to me It is more or less constant rather than transitory, although it sometimes becomes aggravated However, it does not become much greater than it is at the present time I believe that it is of allergic origin

DR. D M SIDLICK The patient's statement that the swelling has never disappeared would speak against the diagnosis of angioneurotic edema I think that it is lymphangioma circumscriptum congenitale

DR. HERMAN BEERMAN I suggest the possibility of elephantiasis nostras

DR FRED D WEIDMAN I thought that maybe it was an example of so-called woody edema, which appears generally near foci of infection, for example, on the cheek where there are underlying foci of sinusitis If there were apical abscesses I suppose that would strengthen that idea So far as I can learn, there are no nearby foci of infection to explain woody edema I think that all the members feel that the enlargement of the lip is due to fluid of some kind I think that the swelling is diffuse lymphangioma circumscriptum congenital It is in one of the common positions for this lesion Usually, it is true, it occurs in persons much younger than this patient.

DR. ISADORE ZUGERMAN The enlargement is confined to the area of hair growth The ends of the lip are not involved None of his physicians were able to do anything for him He is extremely uncomfortable, and I do not know what to do for him I should appreciate suggestions

DR FRED D WEIDMAN I think that the diagnosis will have to be settled first

DR ISADORE ZUGERMAN The possibility of trauma was considered I asked if his lip had been punched at any time He is not a boxer, and he said that he had never been struck

**Pemphigus Vulgaris** Presented by DR MEYER L NIEDELMAN

P M, a white man aged 53, presents patchy denudations of the epithelium in the mouth, especially on the soft palate A few of the lesions are covered with a white membrane and resemble leukoplakia There is crusting of both nares Scattered over the trunk and the face are numerous crusted lesions, the remains of previous bullae Six months ago the patient first noted what he called boils in the left axilla His family physician said that they were bullae which subsequently underwent suppuration Shortly thereafter painful oral lesions developed, which became vesicular At first localized on the tongue, they later spread to the rest of the buccal mucous membrane and the soft palate Then both flaccid and tense bullae developed on various parts of the trunk These appeared suddenly on normal skin, ruptured and formed crusts He has lost about 10 pounds (4.5 Kg) in the last two months because of inability to eat, due to the painful oral lesions One month ago bullous and vesicular lesions developed in the nose, which have become crusted and have caused difficulty in breathing The patient has been treated by various physicians for Vincent's infection of the mouth and avitaminosis

DISCUSSION

DR BERNARD L KAHN I had a similar case in which the eruption cleared completely with penicillin

DR CARROLL S WRIGHT I think that the more one sees of pemphigus, the more one realizes that there is no single remedy that works in all cases Years ago Dr Schamberg became enthusiastic about colonic irrigations After employing them for some time, 1 patient recovered and lived for three years Another woman did likewise for ten years Both patients were Jewish In other than these 2 cases, my associates and I saw no more good results from colonic irrigations Then came the vogue of treatment with iron cacodylate and coagulin Later we heard from Dr Ludv of good results with the use of thiamine We have a patient at present who remains absolutely free of lesions as long as she takes acetarsone Still, the last patient I saw treated with acetarsone had an extremely malignant eruption and died It cannot be said that any one remedy will work in every case I think that is what is going to happen with penicillin It is worth trying, however, I had a patient recently who could not take sulfonamide drugs by mouth, we used to spray her with a sulfonamide lotion (5 per cent sulfathiazole), and every lesion healed She went home and lived for eight months before suffering a recurrence The sulfonamide lotion was again used, but it was ineffective and she died

DR ISADORE ZUGERMAN I noticed the extensive involvement of the patient's mouth and the bad condition of his teeth I suggest that he receive all necessary dental care It may be of help to him

DR JOHN F LENTZ I had 1 patient who died in spite of and another who responded fairly well to the use of sulfonamide drugs in powder form The latter patient willingly donated his blood to the former, but it did not help

DR MEYER L NIEDELMAN Penicillin has been used in treating pemphigus without any effect on the disease Patients with lesions in the mouth fail rapidly in health, and the prognosis is bad The patient previously mentioned by Dr Wright first had lesions in his larynx, six months later he had lesions in the mouth and then on the body He died five days after the explosive appearance of the generalized cutaneous lesions

DR D M SIDLICK I do not think that it is a safe practice to base a diagnosis simply on lesions in the mouth for the reason that even lesions that appear bullous are not always proved to be pemphigus

## Dermatofibroma (Fibrosarcoma?) Presented by DR SIMON KATZ

J C J, a white man aged 63, presents in the lumbosacral region a sclerotic plaque measuring 25 by 40 cm, in which there are several painless firm reddish nodules, some of which are elevated above the surface. The plaque is only slightly adherent to the subcutaneous tissue. When first seen, the plaque was bluish and contained several purplish nodules in the center, but the picture has changed since the application of roentgen ray therapy. In 1912, a carbuncle developed over the lumbosacral region. A salve was applied, and healing took place in four weeks, leaving two raised scars. Fifteen months ago the areas became larger, and a small ulcer appeared in the center. It never itched and was never treated by any physician. The patient has a history of recurrent furunculosis from the age of 15 to 53 years.

A roentgenogram of the teeth showed no infection. The urine in November 1944 was normal. The serologic reaction of the blood for syphilis was negative on Sept 25, 1944. On November 15, the sugar and urea content of the blood were 109 and 11 mg respectively per hundred cubic centimeters of blood. A blood count showed no significant abnormalities.

On Oct 7, 1944, Dr Weidman reported on the first biopsy as follows: "The epidermis was normal. The corium was almost entirely occupied by newly formed bundles of fibrous tissue. The nuclei within the bundles were numerous and of mature type. There was not the slightest evidence of sarcomatous change."

The report of the second biopsy was as follows: "The epidermis was normal except for secondary atrophic changes. The corium was thickened to a distance of about 8 mm by a solid mass of tumor tissue. There were not any remains of the collagenous tissue, but a few sweat ducts still remained. The tumor infiltrated extensively into the subcutaneous fat. As a basis for the tumor there was a whorling stroma of moderately dense fibrous tissue which was fairly richly vascularized. On it, great numbers of spindle cells were placed, the nuclei of many of these were deformed, sometimes they were even stellate. In spite of the fact that the tumor involved the subcutaneous fat, I did not believe that it was malignant. It was true that the tumor cells were closely placed, but at no position were they of the richly chromatinized type which should have appeared had they been sarcomatous."

From Oct 26 to Nov 17, 1944, the patient received roentgen ray therapy—100 kilovolts, 5 milliamperes, at a distance of 30 cm, with a 4 mm aluminum filter, 200 r per treatment, two to three times weekly, for a total of 2,000 r (erythema dose equals 600 r).

## DISCUSSION

DR SIMON KATZ: When this patient was first seen, he had a number of reddish and bluish nodules in this plaque, which gave it the appearance of a fibrosarcoma. The first biopsy section did not show any evidence of malignant growth. It was suggested that another section be taken from one of the bluish nodules, but neither did the second section show any evidence of malignant change. In the absence of highly chromatinized cells a diagnosis of fibrosarcoma could not be made. After roentgen ray therapy most of the nodules disappeared. I noticed tonight that one of the nodules is returning. The best treatment would be wide excision, which the patient has refused.

DR FRED D WEIDMAN: The lesion has behaved like a fibrosarcoma, but histologically the particular tissue I looked at did not show any sarcomatous features even though it did come from the bluish part. Maybe those bluish parts had been irradiated previous to being submitted to the second biopsy. That might account for the adult type of cell that appeared at the second biopsy. I recall that in the first case of this type that I ever studied the entire lesion was excised and there were certain parts which showed only scar tissue where the lesion had regressed spontaneously, always to crop up in some other places. In histologic study so much depends on the part of the lesion that has been selected and whether it has been previously treated.

# Hodgkin's Disease of the Skin Without Demonstrable Systemic Involvement Presented by DR LOUIS GOLDSTEIN

C S, a white woman aged 38, whose father died of tuberculosis fourteen years ago and whose mother died of pneumonia, and a sister of cancer of the breast, presents on both upper extremities, the lower part of the back and the upper part of the thighs a number of discrete, scattered nodules of various sizes, the largest of which is the size of a split pea. The color of some nodules is that of normal skin, while a few show inflammatory changes with a tendency to desquamation. One may also see light brown pigmented spots, the remains of lesions that have undergone involution. The patient, a frail young woman of the viscerotropic type, had a hysterectomy for a fibroid tumor of the uterus seven years ago. She had an attack of pleurisy six years ago. She is also allergic to grasses.

The disease started seven years ago on the upper extremities as a few discrete nodules, the color of which was that of normal skin. The nodules gradually became inflammatory. The surface epithelium would desquamate, and finally the lesions would disappear, leaving behind brown pigmented spots. During these seven years she has never been free of the lesions. As the old ones would heal, new crops would appear. Itching has been slight, but more intense when a new lesion appeared. Some nodules in their terminal stages showed a tendency to superficial ulceration.

The spleen was not palpable. The liver showed no enlargement. The right submaxillary gland was palpable, and a nodule the size of an almond was felt in the right axilla. The inguinal nodes were slightly palpable.

The serologic reaction of the blood for syphilis was negative. The urine was normal. The sedimentation rate ranged from 11 to 15 mm in one hour. The sugar content of the blood was 84 mg and the urea nitrogen 14 mg, per hundred cubic centimeters of blood. The tuberculin test with purified protein derivative, 0.00002 Gm, gave a positive reaction. Complete blood cell counts on Dec 7, 1944 and May 7, 1945 gave essentially normal findings.

## DISCUSSION

DR D M SIDLICK This is a case in which the diagnosis depends entirely on the laboratory studies. Clinically the eruption certainly does not have any resemblance to Hodgkin's disease of the skin, and the history also is a bit contradictory. She has had the eruption for the past seven years. I do not know what the diagnosis is, but clinically the eruption does not appear to be Hodgkin's disease of the skin.

DR SIMON KATZ Twelve per cent of the patients with Hodgkin's disease of the skin do not show any glandular adenopathy, sometimes for a long time. In other words, one can have cutaneous lesions in Hodgkin's disease of the skin before any glandular adenopathy develops.

DR FRED D WEIDMAN The diagnosis histologically is made on the basis of what the sections show. It does not mean that the histologist is going to discard all the clinical circumstances and say This must be Hodgkin's disease of the skin because the picture under the microscope is that of Hodgkin's disease. I agree entirely with Dr Sidlick that clinically this is not a case of Hodgkin's disease of the skin in its typical expression. At the same time, I should like some constructive criticism. If the eruption is not Hodgkin's disease of the skin, what is it? This woman has a straight chain of large nodes in her left groin and one node, the size of a pigeon's egg, in her right axilla. She is pale and thin and has a much fissured tongue, like that of Vincent's syndrome. She seems anemic. I think that if she is to be studied the investigation should be along the line of one of the leukemias. There are typical Sternberg-Reed cells, but in this patient there is not the hyperplasia of the epidermis that has always been described in cases of eosinophilic granulomas of the skin.

DR BERNARD L KAHN About two years ago I had a patient with fever as the outstanding symptom. Various diagnoses were made at the time. At first the

fever was thought to be typhoid. Finally, a small gland in the patient's neck was removed, and histologic examination proved it to be Hodgkin's disease of the skin. He had no clinical symptoms for about eight or nine months other than pyrexia and enlargement of that gland. He ultimately died of Hodgkin's disease of the skin.

DR REUBEN FRIEDMAN I have a patient who has been seen by ten or twelve consultants in the past two years, all of whom have discussed the question whether or not he has Hodgkin's disease of the skin. My patient has or has had almost everything seen in Hodgkin's disease of the skin but typical Sternberg-Reed cells. The question of making a diagnosis of Hodgkin's disease of the skin without finding typical Sternberg-Reed cells was debated. Tonight we saw a case that appears to have little or nothing other than typical Sternberg-Reed cells to support a clinical diagnosis of Hodgkin's disease of the skin. I am therefore moved to inquire whether the finding of typical Sternberg-Reed cells is in itself conclusive evidence of Hodgkin's disease of the skin.

DR FRED D WEIDMAN The finding of typical Sternberg-Reed cells is not pathognomonic of Hodgkin's disease, they are nothing more or less than monocytes. When seen in combination with the other tissue changes, they support the diagnosis. In Spiegler-Fendt sarcoid, time and again one will see a monocyte which will be identical with one of the multinuclear forms of Sternberg-Reed cells. Such cells can be both mononuclear and multinuclear. In Spiegler-Fendt sarcoid one can see good examples of the multinuclear Sternberg-Reed cell.

DR LOUIS GOLDSTEIN I made the diagnosis in this case of "Hodgkin's disease of the skin without systemic involvement" on the basis of the histologic report of Dr Weidman. It is known that Hodgkin's disease of the skin may at times manifest cutaneous lesions, some of which are specific histologically and others nonspecific. This case is puzzling. If the eruption is Hodgkin's disease of the skin, then, since she has had it for eight years and that period constitutes the average life expectancy for this disease, is it possible that this is the first case of such long duration of Hodgkin's disease of the skin without systemic involvement?

**A Case for Diagnosis (Leukemia? Scabies?)** Presented by DR FRED D WEIDMAN and (by invitation) DR HARRY BOCKUS

L G, a white woman aged 23, well nourished, somewhat pallid, with febrile rashes, presents on both arms, but not the fingers, scores of minute excoriated papules. They are distributed diffusely. On both lower extremities there are similar but larger lesions, together with residual pigmentary macules. A number of thick-walled pustular blebs are distributed on the upper part of the thighs and the lower part of the back. The abdomen is scarcely involved. Itching is severe enough to keep the patient awake at night. The liver is enlarged about 2 cm below the costal border, the spleen is progressively enlarging. Only one lymph node, in the left groin, is enlarged. She has colitis, with occult blood in the stool.

The erythrocytes have ranged down to 3,000,000, and the leukocytes, to 5,100, blood cultures failed to show growth of any organism, and the differential count was normal. The serologic tests for typhus, brucellosis and paratyphoid gave negative results. There were no malarial parasites. Roentgenograms showed that the chest, the skull and the shoulder were normal. Hemolytic streptococci and non-hemolytic staphylococci were isolated from some blebs.

The report on an examination of bone marrow, March 15, 1945, was as follows: "There was no evidence of blood dyscrasia." The report on an examination of the lymph nodes on May 14, 1945 stated: "Histoplasmosis was eliminated. Although the normal architecture was destroyed by massive lymphocytic proliferation, there was no other evidence of Hodgkin's disease of the skin. Many mitotic figures suggested lymphosarcoma."

Penicillin and penicillin ointment caused regression of the cutaneous lesions. She has received transfusions of blood and blood plasma. She has been given a high vitamin diet and treatment with preparations containing iron.

## DISCUSSION

DR FRED D WEIDMAN Objectively this eruption suggests scabies, but it is remarkably sparse on the abdomen and the sulfur ointment did not cure the patient. Moreover, at one time the eruption was present on the forehead. I prefer a tentative diagnosis of some leukemoid pathosis (including Hodgkin's disease of the skin). Of course it would have to be aleukemic. The itching appears to exclude a bacterid. Unfortunately, the specimen from the lymph node was not a satisfactory one. It was so mangled that too much credence cannot be given to what it shows in respect to Hodgkin's disease. The internist has not made a diagnosis in this case and calls on the dermatologists for help. I think it is natural in the case of a patient who shows splenomegaly and hepatomegaly and at least one enlarged node that one should think of the possibility of leukosis. The eruption might be an id. I think that one can eliminate scabies satisfactorily, and I do not think that the eruption is urticaria papulosa.

DR EDWARD F CORSON I think that the eruption is a factitial dermatitis because in answer to my questioning the patient insisted that she did not pick the lesions or make any applications to them, and yet at a number of points there were highly pigmented scars. To my mind that is evidence of factitial dermatitis. Many of the pigmented lesions might readily be the end results of the fresh ones seen tonight.

DR SIMON KATZ I believe that this eruption represents a systemic infection with local cutaneous phenomena. On the buttocks there are several lesions showing gangrenous centers. I think that the patient should be studied from a systemic angle. I understand that penicillin therapy has done her much good.

DR J M SCHILDKRAUT, Trenton I think that she has simply a low grade staphylococcic infection.

DR FRED D WEIDMAN There is a certain orderly distribution to the lesions that does not seem to go with dermatitis factitia. Her arms are affected from the shoulders to the wrists on each side, and so are the lower extremities, but practically none of the abdomen is involved, which I think is a point against a diagnosis of dermatitis factitia.

### Dermatitis Herpetiformis Caused by Stasis Dermatitis Presented by DR LOUIS GOLDSTEIN

T S, a white woman aged 60, obese, with an acromegalic facies, presents a rosacea-like flush in the midvertical third of the face. On various parts of the body, especially on the lower part of the abdomen, the buttocks and the upper part of the thighs, she shows numerous excoriations and grouped papules, some with excoriated tops. The entire body, particularly the covered parts, show pigmented post-traumatic spots resembling freckles. The ankles show indurated eczematoid dermatitis (stasis dermatitis). The feet present evidence of dermatophytosis. The legs have decided varicosities. The patient in childhood had eczema which cleared up at puberty. She had dermatitis of the forearms in 1927 and 1928, caused by "nerves." The patient's mother died of carcinoma. The present disease began four years ago with an eczematoid eruption of the ankles. A year later a generalized dermatitis developed, with severe itching and burning and a sensation of crawling under the skin. This has persisted to date with few remissions. Worry has provoked exacerbations.

The serologic reaction of the blood for syphilis was negative. A hemogram showed an eosinophilia (14 per cent). The urine was normal except for a slight trace of albumin and some leukocytes. The basal metabolic rate was +11 per cent. A patch test with 50 per cent potassium iodide in petrolatum produced a decided reaction.

The patient has been treated with ultraviolet irradiation and various local applications and has taken sulfapyridine internally since last March. She has improved greatly but occasionally suffers a relapse, though less severe than before.

## DISCUSSION

DR MORRIS MARKOWITZ I grant that the patient has stasis dermatitis. However, I do not see the grouping and vesicles of dermatitis herpetiformis, and there is hardly any pigmentation. I think that the eruption looks like stasis dermatitis plus scabies.

DR CARROLL S WRIGHT I think that this eruption might be classified as a neurodermatitis. I asked the patient whether she thought there was any relation between her eruption and the state of her nerves. She replied that she had not thought of it before, but at one time last winter when she was practically free of the eruption her daughter called her up from New Mexico and said she wanted to come home. The patient at once started to itch and before morning was covered with patches of dermatitis. This certainly seems to me a case in which the psyche plays a part.

DR BERNARD L KAHN It is more like a case of lichen simplex.

DR ISADORE ZUGERMAN The lesions on the ankles do not look like stasis dermatitis, they resemble neurodermatitis.

DR LOUIS GOLDSTEIN An "id" eruption secondary to the disease on her ankles was considered as a diagnostic possibility. At that time the ankles were the sites of an exudative dermatitis with secondary infection. Although the patient may be nervous, she had many exacerbations without any apparent reason. In her case I believe that the cause of her eruption resides in the stasis dermatitis of her legs. Whenever that gets worse, she breaks out in a generalized eruption resembling dermatitis herpetiformis.

Parasitic Infection? Scabies? Presented by DR BERTRAM SHAFFER and DR HERMAN BEERMAN

M B a white woman aged 67, apparently healthy, presents papular lesions and some excoriations on the trunk and the extremities. She was first seen on Feb 1, 1945, with a pruritic eruption of several months' duration, which became worse at night. The patient's niece and grandniece had been successfully treated for scabies prior to her first visit. She has osteoporosis of the spine, for which she wears a brace. However, the brace has not been worn for six weeks.

A complete blood count revealed 94 per cent hemoglobin, 4,990,000 erythrocytes and 6,200 leukocytes, with 66 per cent polymorphonuclear leukocytes, 28 per cent lymphocytes and 6 per cent monocytes. Two biopsies have been performed, with no definite diagnosis.

Temporary improvement followed the use of benzyl benzoate emulsion, a sulfur ointment and Yonona, a lotion containing 2 per cent rotenone.

## DISCUSSION

DR FRED D WEIDMAN There is something distinctive in the histologic picture in this case. There is a large group of dilated lymphatic spaces surrounded by a broad zone of inflammatory reaction. When I saw them, I thought of the reactions I saw in some sections of creeping eruption, except that these spaces are much larger and more clearcut. These occur deeply, in the midcorium or even below. I think that all dermatologists realize that those are deep spotty lesions, such as might be seen in urticaria pigmentosa. There is no question about its being lymphangitis. Whether a parasite is responsible for that or not, I do not think anybody can say. I do not know of any parasite that produces such an eruption.

DR I M SCHILDKRAUT, Trenton, N J I thought that clinically it looked like pityriasis lichenoides et varioliformis acuta.

DR EDWARD F CORSON There is a uniformity about the lesions which is against a diagnosis of scabies. Nearly all are of the same size and have the same characteristics. The eruption might possibly be papular urticaria or prurigo mitis.

**Lupus Vulgaris** Presented by DR MEYER L NIEDELMAN

M J a white woman aged 60, presents on the right side of the forehead and scalp, the right side of the face, the left side of the chin and the neck and both gluteal areas large, sharply demarcated, circumscribed, erythematous, reddish brown patches. These patches are not elevated. The borders are hyperpigmented and show numerous apple jelly nodules. There are areas of atrophy scattered throughout the lesions. The lesion on the right frontal area extends into the scalp, showing an area of total alopecia extending about 2 inches (5 cm) from the hair line. There are no lesions of the mucous membranes. The patient complains of being continuously weak, with inability to do her ordinary housework. She has been under treatment by various competent dermatologists. About thirteen years ago a small lesion developed on the left side of the chin, which subsequently spread. Then lesions developed on both gluteal areas. About four years ago similar lesions developed on the right side of the forehead, the scalp and the right side of the face. The patient came to the United States at the age of 13. She has two brothers and two sisters, both well. There is no family history of tuberculosis.

The patch test with tuberculin elicited a strongly positive reaction. A roentgenogram of the chest was negative for tuberculosis. A complete blood count revealed 68 per cent hemoglobin, 3,200,000 erythrocytes and 4,950 leukocytes, with 51 per cent neutrophils, 47 per cent lymphocytes and 2 per cent monocytes. The urine was normal. The serologic reaction of the blood for syphilis was negative. The blood sugar level was 99 mg per hundred cubic centimeters. The report on the biopsy specimen was "consistent with lupus vulgaris."

The patient has been given the Gerson diet, large doses of vitamin B complex intramuscularly and injections of crude liver extract. Locally she has been given 10 per cent pyrogallol in petrolatum.

## DISCUSSION

DR D M SIDLICK I think that it is rather unusual for lupus vulgaris to be present for thirteen years without showing greater destructive changes than are found in the present case. Despite the fact that the lesions do cover considerable ground, the only destructive change evident clinically is atrophy. I do not think that the eruption is lupus vulgaris. I think that it is lupus erythematosus.

DR CARROLL S WRIGHT Dr Gross and I saw this patient some years ago and we both thought that she had lupus vulgaris. At that time the patches were not more than one-third the size they are now. The eruption has therefore extended rather rapidly for lupus vulgaris. At that time we gave her a salt-free diet and treated her with gold and solid carbon dioxide. We had her under observation for six or eight months, and the lesions did not increase in size during that time. I still feel that the disease is lupus vulgaris, though somewhat atypical.

DR MEYER L NIEDELMAN I do not believe that there is any question about the diagnosis, although this may fit into the type known as lupus vulgaris erythematosus. It is rather unusual to start at the age of 47, and the lesions have progressed rapidly in a period of three years. She also had two large areas in the gluteal region which show typical apple jelly nodules.

DR CARMEN C THOMAS Dr Urbach treats lesions of this sort with pyrogallol and irradiation, with good results.

DR MEYER L NIEDELMAN I have used pyrogallol in 10 per cent strength. This caused a tremendous inflammatory reaction, which lasted six weeks before it quieted.

**Acrokeratosis Verruciformis (Hopf)** Presented by DR MEYER L NIEDELMAN

M D, a white woman aged 37, and her son, P D, aged 17 years, present lesions on the dorsal and the palmar surfaces of the hands and on the dorsa of

the feet. The lesions are also present for several inches above the wrists and the ankles. Most of these verruca-plana-like papules are discrete, but many are confluent. They vary in diameter from the size of a pinpoint to 4 mm. Some are elevated up to 1 to 2 mm above the surface of the skin. The lesions on the palms and the soles are few in number and almost disappear as they approach the center. There are no subjective symptoms. Both patients have keratoses of the palms and the soles. Their color varies from a flesh pink to a light brown. The lesions on the dorsum are flat and smooth, although a few are verrucous. Many are polygonal and resemble lichen planus. Even the confluency of the papules does not destroy their individual configuration. On biopsy the lesions cut with some resistance, resembling fibrous tissue. Many of the lesions have a sheen. The lesions on the palms and the soles appear embedded and are "shotty" to touch. They are discrete and are better felt than seen. When the skin is put on the stretch, one can see a papule extending above the surface. This appearance is probably due to pressure. P. D. consulted me because of warts on his hands. He said that these had appeared at or about 9 months of age, according to his mother. When he was questioned further, it was found that his mother and two sisters have a similar disease. In all the patients the lesions had appeared between 6 months and 1 year of age. There is no consanguinity. There are 14 patients in one family.

The serologic reactions of the blood for syphilis, a complete blood count, the results of urinalyses and the blood sugar level were normal. The basal metabolic rate of M. D. was —15 per cent.

The biopsy was reported by Dr. Weidman as follows: "The reaction was one of the purest examples of acanthosis and hyperkeratosis that could be imagined. On the surface of the skin the stratum corneum appeared purely as hyperkeratosis—not a trace of parakeratosis. It was excessively thick, three or four times the thickness of the rest of the epidermis. Correspondingly, the stratum granulosum was thick and conspicuous, and the prickle cells were moderately hyperplastic. The general configuration of the interpapillary pegs was well maintained. At the most, they were only broadened or thinned, and all of them extended downward to a uniform level. The corium exhibited no pathologic changes. The diagnosis was *acrokeratosis verruciformis*."

#### DISCUSSION

DR. MARJORY K. HARDY: I presented the cousins of these patients about two and a half years ago. At that time the woman was pregnant, and the child of that pregnancy, at the age of 13 months, had developed similar lesions. The male cousin of this woman was originally seen at the Philadelphia General Hospital about 1941, and his disease was diagnosed by Dr. Gross. A number of such cases had previously been presented at the Atlantic Dermatologic Conference in Baltimore.

DR. FRITZ CALLOMONT (by invitation): This case of *acrokeratosis verruciformis* is most significant with regard to the occurrence of this cutaneous disease in 14 members of three generations of one family.

## Book Reviews

**Skin Diseases, Nutrition and Metabolism** By Erich Urbach, M D, Associate in Dermatology, University of Pennsylvania School of Medicine, Chief of Department of Allergy, Jewish Hospital, Philadelphia, with the collaboration of Edward B LeWinn, M D, Associate in Medicine, Jewish Hospital, Philadelphia First edition, cloth Price \$10 Pp 634, with 266 illustrations New York Grune & Stratton, Inc, 1946

The book is arranged in five parts Part I is concerned with the biochemistry and physiology of the skin, with a particular attempt to show the influence of diet on various constituents of the skin and metabolism Part II covers the dermatoses due to malnutrition, especially vitamin deficiencies and allergies Part III attempts to coordinate gastrointestinal disturbances with cutaneous diseases Part IV discusses some dermatoses specifically and points out the possible dietary treatment for these diseases Part V gives rather complete nutritional tables

This book is a compilation of material in which dermatologic diseases are studied from a new approach, that is, much of the material is covered in previous texts and in the literature, but no textbook which confines itself strictly to the relationship of metabolism and nutrition to diseases of the skin has been published before Insofar as a new approach to dermatology is always of interest and value, the book is therefore, worth while, however, much of the material and many of the conclusions are too indefinite and of too doubtful use to warrant the authority granted them by publication in a textbook As an example, the low fat diet as a treatment for psoriasis is discussed at length and recommended somewhat too vigorously considering the lack of definite results in the practical use of such a routine Another example of this type is the great amount of space devoted to the use of "propeptans" in the treatment of urticaria and atopic eczema, whereas the general use and availability is limited Such treatment is not mentioned in the latest edition of such texts as those by Sutton and Sutton or Ormsby and Montgomery, and even in an allergy text such as Sulzberger's the use of "propeptans" is covered by a small footnote

The whole text would be more valuable if instead of all the literature written on the subject, especially that in foreign languages, being quoted any statements had been qualified directly or omitted if not found to be generally true This is illustrated by the quotation from Hoff and Riehl that chloasma and other types of pigmentation respond to huge doses of vitamin C This effect of vitamin C is dubious, to say the least, and the use of vitamin C in this way is not even mentioned in the standard textbooks

Many other statements are given the authority of being printed in a text when actually the results claimed are indefinite or at least variable This is especially true when the foreign language literature is cited, and, except for the section on vitamins, literature in non-English language makes up 57 per cent of the bibliography, whereas in the sections on vitamins only 18 per cent of the bibliography is from sources in a foreign language In this connection, it is interesting to note that the most valuable and really worth while part of the text covers the relationship of vitamins to cutaneous diseases

A part of the text that is of interest and may be useful at times consists of numerous tables Here, at least, is a readily available reference source for information which covers subjects as diverse as conversion of grains into grams and the normal values for various lipids in the skin and plasma

As an editorial point, it would be better if the "Standard Nomenclature of Disease" had been followed exactly and such terms as "lichen ruber planus" for "lichen planus" and "dermatitis" for "eczema" had not been used

On the whole, the subject has been covered thoroughly, and if the material had been presented as a monograph with bibliographic references rather than as an authoritative text it would have been better

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## PSYCHOSOMATIC FACTORS IN DERMATOSES

A Critical Analysis of Diagnostic Methods of Approach

FRANK E. CORMIA, M.D.\*

NEW YORK

THE OBSERVATION of dermatoses in military personnel, especially combat soldiers, offers an unparalleled opportunity for study of possible psychosomatic factors. Army life differs from that prevailing in civilian communities by the frequency and intensity of situations that lead to basic conflicts. The rigidity of the environment does not permit modifications so necessary for the continued functioning of persons with borderline psychoneurotic or psychopathic personalities, while the replacement of the protection of familial or domestic life by an impersonal domination leads to frequent conflicts with authority. Moreover, the threat of combat to the basic instinct of self preservation results frequently in a permanent conflict, which can be solved only by the removal of a soldier from the threat of death or injury. In many instances a soldier solves his problem by the development of psychosomatic diseases, the cure of which is obtained only with extraordinary difficulty, because of an active desire to remain sick. The direct threat to life and the reaction of a person to authority far overshadow subservient instincts, and, while conflicts in the sexual and other spheres do occur, they are less common.

Consequently, it is to be expected that there will be a great increase in the number of patients with psychosomatic cutaneous disorders and that the working out of their nature will be greatly simplified by the intensity of the precipitating stimuli. And this is exactly what does occur. During a two year tour of duty in the European Theater of Operations about 100 patients with psychosomatic dermatoses were seen. Prior to D day psychosomatic disease made up but 3 per cent of the total. Subsequent to that date the proportion increased to 10 per cent. Of equal significance and indicative of the chronic, treatment-resistant nature of this type of illness, was the fact that 25 per cent of all patients returned to the Zone of the Interior as presenting failures in treatment had a psychosomatic type of dermatosis. Following V-E

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day the number dropped precipitously, but it is significant that in the days of uncertainty incident to redeployment a gradual increase was again noted. The present paper is a study of this group of patients, with a critical analysis of the diagnostic and therapeutic value of the various methods of approach to the problem.

#### GENERAL CONSIDERATIONS

The present status of the understanding of the underlying mechanisms and psychodynamics of psychosomatic dermatoses is still little less than chaotic. It has been aptly compared by Rogerson to "an unconsummated marriage between a ghost and its integument."<sup>1</sup> There are persons who express a healthy skepticism of the concept of neurogenic dermatitis.<sup>2</sup> Sulzberger<sup>2</sup> considered that nervousness in the presence of a dermatosis could be incidental or be produced by the same factor but that in the majority of instances it was the result of pruritus, insomnia or worry over the possibility of disfigurement or of conjoint economic problems. Other authors,<sup>3</sup> on the contrary, have insisted that psychic factors are important in from 5 to 15 per cent of patients with dermatoses and have written extensively to prove their point. While this controversy has been in progress, a good deal of work has been done on the intermediary physiopathologic mechanisms present in "psychogenic" dermatoses. Specifically, Grant and his associates<sup>4</sup> have shown that urticaria can be provoked through cholinergic, efferent peripheral nerves, and van de Erve and Becker<sup>5</sup> have studied the functional state of the skin in patients with neurodermatoses. In a patient with convulsions complicated by

1 Forman, L. Watt, A., Wittkower, L., and others. Unpublished material read at the Annual Meeting of the British Association of Dermatology and Syphilology, July 6-7, 1945.

1a O'Leary, P., in discussion on van de Erve and Becker.<sup>5</sup> Goldsmith, W. N. Significance and Treatment of Itching, Practitioner **142** 36, 1939. Peck, S. M., in discussion on Lynch, Hinckley and Cowan.<sup>11</sup>

2 Sulzberger, M. B. Dermatologic Allergy, Springfield, Ill., Charles C. Thomas, Publisher, 1940.

3 (a) Stokes, J. H., and Beerman, H. Psychosomatic Correlations in Allergic Conditions. A Review of Problems and Literature. Psychosom. Med. **2** 438, 1940. (b) Klauder, J. V. Psychogenic Aspects of Skin Diseases, J. Nerv. & Ment. Dis. **84** 249, 1936. (c) Kreibich, C. Neurodermatitis und Neurodermie, Arch. f. Dermat. u. Syph. **152** 672, 1926. (d) Becker, S. W., and Obermayer, M. E. Modern Dermatology and Syphilology, Philadelphia: J. B. Lippincott Company, 1940. (e) Rogerson, C. H. Psychological Factors in Skin Disease, Practitioner **142** 17, 1939.

4 Grant, R. T., Pearson, R. S. B. and Comeau, W. J. Observations on Urticaria Provoked by Emotion, by Exercise and by Warming the Body, Clin. Sc. **2** 253, 1936.

5 van de Erve, J. M., and Becker, S. W. Functional Studies in Patients with Neurodermatoses. I. A. M. A. **105** 1098 (Oct. 5) 1935.

urticaria, I was able to reproduce the cutaneous lesions without the convulsions by using electrical stimulation through the leads of the electroencephalograph, so placed that the maximum current passed through the thalamus. Interesting as these and related observations are for the verification of the neurogenic origin of a dermatosis, they can be of little aid in the management of the individual case, which in the last analysis is due to psychic trauma and conflict. Furthermore, the eradication of symptoms by forcible means, i. e., the injection technic for pruritus and or the neutralizing of cholinergic effects in the skin, may rob the patient of a means of solving conflict without removing the basic underlying cause. In a personally observed case, arrest of intractable pruritus and by the injection technic resulted in the development of a severe psychoneurosis. More recently, the studies of Dunbar<sup>6</sup> have stimulated research on the correlation of psychogenic dermatoses and personality types.<sup>7</sup> While this modern scientific tendency to pigeonholing and classification has undoubted merit, it too has but limited applicability in analysis of individual cases. It does not identify the basic factors producing conflict and can be utilized only in conjunction with more fundamental methods of study, to be presently discussed.

#### FUNDAMENTAL RELATIONS BETWEEN THE PSYCHE, SOMA AND SKIN

As the eye is the mirror of the soul, so may the skin reflect the psychosomatic personality and its struggles with life. Conflict and tension are produced, and they may be partially relieved by the development of somatic symptoms. These symptoms are an expression of and a defense against conflict. The factors responsible for organ selection, however, are but imperfectly understood. Why, for example, should some patients with hysteria become paralyzed in an extremity or suffer from loss of vision, while dermatitis factitia develops in others? Or why should an acute anxiety manifest itself in some instances as an anxiety neurosis and in others as severe urticaria? In an attempt to explain these inconsistencies, Weiss and English<sup>8</sup> spoke of "organ language" by which a mute (repressed) patient expresses himself. A patient with neurotic vomiting is trying to "relieve himself" of a personally nauseating or intolerable situation, one with hysterical blindness in shutting out unwelcome sights.

6 Dunbar, F. Psychosomatic Diagnoses, New York, Paul B. Hoeber, Inc., 1943.

7 (a) MacKenna, R. M. B. Psychosomatic Factors in Cutaneous Diseases, *Lancet* 2: 679, 1944. (b) Forman and associates.<sup>1</sup>

8 Weiss, E., and English, O. S. Psychosomatic Medicine, Philadelphia, W. B. Saunders Company, 1943, p. 10.

The symbolism of symptoms is nowhere better shown than in the skin. It is expressed both in the type and in the localization of the dermatosis. The skin has the power of expressing many bodily emotions, including those of worry (picking), anxiety (pruritus and sweating), fear and anger (urticaria), guilt and shame (blushing and rosacea), hostility, masochism and eroticism (dermatitis factitia) and sexual pleasure (cutaneous masturbation). A patient with urticaria may be "bursting the bonds" of restraint (case 11), pruritus and excoriation may represent a martyr-like expression of a desire to "scratch" a disagreeable environment,<sup>8</sup> while severe dyshidrosis may reveal an unconscious protest against using the hands for an irksome or fearful duty.<sup>7a</sup> Similarly, a patient with rosacea is branded with the permanent guilty flush of self consciousness and social anxiety.<sup>9</sup> A victim of factitial dermatitis (case 13) openly expresses his hate, social resentment and antisocial (destructive) tendencies and at the same time exhibits in obvious fashion his demands for attention and sympathy (narcissism, or self love).

A person also attempts, by the localization of his dermatosis, to point out the portion of his environment with which he is coming in conflict and at the same time to make even more clear the essential nature of the conflict. A patient with generalized pruritus is resentful against his entire environment (case 14), pruritus involving the genital region may be due to sexual conflict (case 3) and pruritus ani may be symbolic of a latent homosexual tendency (case 12). Alopecia areata of the scalp is symbolic of a hole in the head and as such may express inadequacy. This is well shown in the following case.

CASE 1—A sergeant aged 24 had always been a shy, seclusive person, unable to mix well with people or to make friends easily. He had had heavy responsibilities for the preceding nine months and found his job "nerve wracking," with constant trouble with subordinates, clash of personalities, sensitivity to adverse criticism and a feeling of inadequacy. Three months later his hair began to fall out in large patches. More recently, an anxiety reaction, moods of depression and beginning paranoid trends developed. The personality was schizoid in type.

The potentially complex symbolism of localization may be illustrated by brief reference to 3 cases.

CASE 2—A patient aged 28 was a masochistic person of strict Catholic upbringing, a failure in social as well as domestic life. The presence of a frigid, aggressive wife led to conflict in the sexual sphere. Sexual tension and concealed hostility to society were relieved by excoriation of the legs, with the eventual production of typical dermatitis factitia.<sup>10</sup> The localization on the legs was in

9 Klaber, R., and Wittkower, E. Pathogenesis of Rosacea. Review with Special Reference to Emotional Factors, *Brit J Dermat* **51** 501, 1939.

10 Cormia, F. E., and Slight, D. Psychogenic Factors in Dermatoses, *Canad M A J* **33** 527, 1935.

part symbolic of an element of shame and guilt "to put the trouble as far away from consciousness (the head) as was possible"

CASE 3—A patient aged 25 was a young woman with an intermittent, pruritic, eczematoid dermatitis of the vulva. The dermatitis was active only during periods of sexual repression, and its nature was understood clearly by the patient. Specifically, the localization was frankly symbolic of the sexual nature of the conflict.

CASE 4—The patient was a young woman of 25 years with an acute pruritic, eczematoid dermatitis involving the face, neck, upper part of the chest and flexor surfaces of the upper extremities. The patient was immature and frigid sexually because of an excessive, lifelong mother attachment. The dermatitis began mildly with her engagement to a forthright Scotsman, it became extensive and severe on the day of her marriage, and it resulted in a prolonged hospitalization. In this patient the localization was in the "blush" area, as such it symbolized the guilt, fear and shame which accompanied the imminency of the physical consummation of marriage.

The psyche unconsciously selects any convenient locus minoris resistentiae for the cutaneous expression of internal conflict. This point is illustrated in cases 5 and 6.

CASE 5—A private aged 19 had eleven months of Army service and one month of combat, following which he was hospitalized because of a gunshot wound in the left hand. The wound healed in a month's time, but he was then seen because of "skin trouble." Examination disclosed a mild atopic dermatitis which showed no evidence of activity or increase in tissue irritability incident to combat. Scattered over the body, however, was a mild chronic psoriasis, the lesions of which were extensively excoriated (fig 1). Further questioning then revealed that the patient had chronic epigastric distress and recurring headaches. Symptoms of acute anxiety had developed while he was in combat. It can be readily seen that the patient utilized the nontroublesome benign psoriasis (by excoriations) to call attention to his underlying anxiety and fear of combat, which by social taboo could not be expressed in the conventional manner.

CASE 6—An Italian-American sergeant aged 27 had three and a half years of training as a combat machine gunner in the Zone of the Interior. He was then sent overseas, but after four weeks of combat he was hospitalized because of a chronic mild swelling of the posterior aspect of the foot and ankle and a secondary pyoderma. On admission there were a few nodular and plaquelike lesions, with some evidence of a clearing infection. In addition, three fresh, irregularly outlined lesions, obviously self induced, were present. The patient complained of severe pruritus. The past history disclosed that both parents had severe psychoneurosis. The patient had been nervous and excitable and had gastric distress for years. More recently he had become irritable, depressed and asocial. Tremulousness and gross anxiety became clinically manifest while he was in combat. Before and during this period mild swelling of one foot had developed. This became secondarily infected through pruritus and excoriation, which were regarded as an unconscious attempt to remain ill and escape unpleasant reality (combat duty).

Conflict and nervous tension may be reflected in the skin as an increased tissue irritability and excitability. This is nowhere better exemplified than in patients with atopic dermatitis (disseminate neuro-

dermatitis), which has received full attention in the writings of Stokes,<sup>8,9</sup> Becker,<sup>10</sup> Rogerson,<sup>11</sup> Lynch and his associates<sup>11</sup> and many others. A basic personality type has been described, and many patients have been greatly improved by psychotherapy. In some persons, however, the influence of psychogenic factors is not so obvious. The following case therefore, will bear presenting, for the relationship of cause and effect was overwhelmingly conclusive.



Figure 1



Figure 2

Fig 1 (case 5)—Neurotic excoriations in a patient with psoriasis

Fig 2 (case 6)—Neurotic excoriations and chronic pyoderma

CASE 7—A private aged 24 was bothered with severe atopic dermatitis for seven years. During the three years prior to induction he had lived in Colorado and had little or no trouble. Because of the pressure of public opinion he concealed knowledge of his dermatosis and enlisted. The dermatitis became mildly active while he was in basic training and became progressively severe

11 Lynch, F. W., Hinckley, R. G., and Cowan, D. W. Psychosomatic Studies in Dermatology. Psychobiologic Studies of Patients with Atopic Eczema (Disseminated Neurodermatitis), *Arch Dermat & Syph* **51** 251 (April) 1945

while en route to a theater of war. An acute, severe exacerbation supervened while he was in a replacement center behind the lines. On receiving orders to join a front line unit, there developed—and for the first time in his life—severe, acute bronchial asthma.

Increased tissue irritability on the basis of conflict not only may be the predominant or sole factor in the production of a dermatitis but may also predispose to the development of dermatoses from other causes or aggravate them when present. I reported a case of contact dermatitis from a menstrual pad, with clinical manifestations occurring only during periods of severe nervous tension.<sup>12</sup> The combined effect of mycotic sensitization and nervous tension are shown in case 8.

CASE 8—A captain aged 33 had been bothered with mild dermatophytosis of the feet for two years. An occasional single vesicle had been noted on the lateral aspects of the fingers during warm weather (tendency to dermatophytid). News was received that a promotion in rank, long forthcoming, had been denied. Within one-half hour, and without other precipitating cause, an acute vesicular dermatophytid was noted over the fingers of both hands.

Patients with seborrheic dermatitis complicated by an excessive amount of pruritus and eczematization are frequently tormented by deep-seated social conflicts. Severe nervous tension in combat personnel has resulted in the eczematization of several patients with pityriasis rosea, in some instances even tinea versicolor has been accompanied with intractable pruritus.

#### TYPES OF PSYCHOSOMATIC DERMATOSES

It seems advisable to present a detailed classification of psychosomatic dermatosis, first, to enumerate the many conditions which may be due to or complicated by psychosomatic factors and, second, to point out the complexity with which these factors may operate to produce cutaneous manifestations. It will then be seen that any classification, however detailed and systematic it may be, is frequently inadequate and at times downright misleading.

##### I Classification of psychosomatic dermatoses

###### A Disturbances in vascular permeability and control

- 1 Dermographism
- 2 Urticaria
- 3 Component in various dermatoses (e. g., rosacea or acute neurodermatitis of blush areas)

###### B Disturbances in nerve innervation

- 1 Paresthesias
  - (a) Acarophobia
  - (b) Burning tongue, penis or scrotum
- 2 Anesthesia (some cases of dermatitis factitia)
- 3 Pruritus
  - (a) As sole manifestation
  - (b) Complicated by acute eczematoid dermatitis
  - (c) Complicated by lichen simplex chronicus
- 4 Hyperhidrosis (and symmetric erythema of feet)

<sup>12</sup> Cormia, F. E. Contact Dermatitis from Menstrual Pad, J. A. M. A. 107:429 (Aug. 8) 1936.

- C Increased tissue irritability and excitability (multiple etiologic factors)
  - 1 Atopic dermatitis (disseminated neurodermatitis)
  - 2 Seborrheic dermatitis (with excessive pruritus and eczematization)
  - 3 Pompholyx (dyshidrosis) some cases
  - 4 Miscellaneous cutaneous diseases pityriasis rosea, psoriasis, tinea versicolor, impetigo and other conditions
  - 5 Increased susceptibility to contact and other types of sensitization dermatitis
- D Self inflicted lesions
  - 1 Neurotic excoriations of incidental cutaneous diseases (impetigo acne psoriasis and other eruptions)
  - 2 Dermatitis factitia
  - 3 Trichotillomania
- E Disorders of uncertain nosologic status
  - 1 Lichen planus
  - 2 Alopecia areata

Dermographism and urticaria may be purely psychosomatic manifestations (case 10), yet the disturbances in vascular permeability are intermediary mechanisms of a process originating in the nervous system and having its end point in the liberation of histamine-like substances<sup>4</sup> In other instances, both sensitization and psychosomatic factors may be present (case 11) The multiple, if somewhat controversial, background of rosacea,<sup>13</sup> in which the psychogenic type of permanent flushing is but a part, is well known Acute eczematous neurodermatitis, illustrated by case 4, presented features of the first four groups of the classification the lesions were in the blush areas, severe itching was present, increased tissue irritability was manifested by the eczematous changes and secondary excoriations were to be seen

Most dermatoses of psychogenic origin are accompanied with severe intractable pruritus The itching may be the sole manifestation (case 14), if long continued, however, and if a makeshift social adjustment has been made to the underlying conflict, it is complicated ordinarily by lichen simplex chronicus On the contrary, when the precipitating stimulus is more intense and a solution to the underlying conflict cannot be found, an eczematous neurodermatitis may supervene (case 4) Some patients with eczematous neurodermatitis have been sorely plagued by social conflicts over a period of years In this group are included the narcissistic persons described by MacKenna and by Miller<sup>71</sup> and properly classified as psychopathic personalities This type is exemplified by case 9

CASE 9—A private aged 28 had a deep-seated paternal conflict acquired in childhood Hatred of the father was expressed by a frankly expressed hostility and aggression directed against society (symbolized paternal authority) The patient was immature, egotistical and argumentative, he was a trouble maker and a social misfit He had two and one-half years of service in the armored infantry, but after two months of combat duty he was hospitalized because of the present condition When first seen he had completed nearly a year of almost continuous hospitalization The present trouble began at the age of 10, with severe, generalized eczematoid dermatitis, followed by a chronic eczematoid dermatitis of the calves,

13 Stokes, J H *Fundamentals of Medical Dermatology*, ed 7, Philadelphia, Department of Dermatology Book Fund, 1942

which had persisted to the present time. The eruption was characterized by an oozing, excoriated dermatitis confined to a large plaque on each calf. The affected areas were covered with Unna's boots, and the dermatitis cleared completely in a ten day period. The patient was warned against excoriating the areas but frankly refused to stop scratching and predicted the early return of the eruption, regardless of the type or success of therapy. The lesions recurred in all severity after the removal of the protective dressings, as a result of repeated excoriations. Failure of the therapy was due to the patient's antisocial and narcissistic traits, which could not be altered by superficial psychotherapy.

Pruritic eczematoid neurodermatitis has been seen in conjunction with independent areas of lichen simplex chronicus (Vidal) and at times with dermatographism and urticaria. It should be mentioned, in passing, that pruritus is an inconstant feature of self-inflicted lesions. Its presence or absence depends largely on the preponderance of unconscious or conscious motivation in the individual case.

The underlying increased tissue irritability, which is an integral component of the eczematous neurodermatoses, atopic dermatitis and some instances of seborrheic dermatitis, may be present also, as stated, in many miscellaneous diseases. This is well shown in patients with psoriasis. As MacKenna has emphasized,<sup>7a</sup> exacerbations and progression of psoriasis associated with inordinately severe subjective symptoms may be due to "the cumulative effect of a dominating anxiety." Many such instances have been seen in combat soldiers and in others for whom military regimentation had become intolerable.

#### CLINICAL APPROACH TO STUDY OF PSYCHOSOMATIC DERMATOSES

Much of the present confusion regarding the psychogenic origin of certain dermatoses has been due to inadequate methods of study. The essential criteria for the study of this important group are but few. In the first place, the method must be adaptable for use by dermatologists. Secondly, it must not be too time consuming. Lastly, it must uncover the etiologic factors and obtain cures or rehabilitation in a sizable proportion of cases.

*Routine Dermatologic Approach.* The initial function of a dermatologist is the determination of the correct diagnosis. The most important diagnostic criterion is that the symptoms are disproportionally greater than the objective signs of disease. Any patient with "idiopathic" pruritus, either localized or generalized, should be clinically suspected. As before stated psychogenic dermatoses may begin without obvious cause. In many instances, however, there is a history of antecedent trauma or of a benign, ordinarily self-limited dermatosis, such as impetigo. Patients with ill defined dermatitis, especially when lichenification is present, should be carefully investigated. Neurotic excoriations and factitial lesions are of course of obvious significance. When a psychogenic origin is suspected, an attempt should be made

to elicit a causal relationship between any severe conflict and the development of the dermatologic complaint. The adequacy of routine management is illustrated by the following case.

**CASE 10**—A Mexican-American private, aged 27, sustained a superficial wound in action after three years of service and one month of combat. The wound healed rapidly, and he was then sent to the rehabilitation section prior to reassignment to a combat unit. Five days later acute severe urticaria developed without obvious physical cause. Routine questioning disclosed gross evidence of acute anxiety, and he was openly fearful of returning to combat. A diagnosis of acute anxiety state with urticaria was made, and he was reclassified for return to the Zone of the Interior. To observe a possible sedating effect, he was told that he was being sent home. Within ten seconds there was a dramatic involution of the lesions. Arrest became permanent after a few minor recurrences during the next two days. No symptomatic treatment was administered.

Dermatologic management of psychosomatic dermatoses is common sense management, as stressed by Michelson.<sup>14</sup> The use of bland, symptomatic therapy, combined with a kindly, sympathetic attitude of the physician and the establishment of a good rapport may serve as a psychologic crutch while a patient works out the solution to his conflicts. All too frequently, however, this type of therapy helps to convince a patient of the physical nature of his complaints, and he makes the rounds of the physicians, finally as a chronic invalid with a fixed psychosomatic dermatosis.

*Dermatologic-Psychiatric Approach*—Recent investigators have adopted a combined dermatologic-psychiatric approach to the study of psychosomatic dermatoses. This method has undoubted value, especially when a patient exhibits trends of a psychoneurotic or psychopathic personality. After initial dermatologic studies, an evaluation of the neuropsychiatric status is made, following which the psychiatrist attempts to identify underlying conflicts and to equate them to the chief complaint. The value of this method is illustrated in case 11.

**CASE 11**—*Routine History*—A patient aged 27 years had two and one-fourth years of Army service, with three weeks of actual combat prior to fracture of the thigh as a result of a shrapnel wound. Intramuscular penicillin therapy was given for nine days because of secondary sepsis, following which time severe urticaria and angioneurotic edema supervened. Routine physical examination disclosed only the presenting condition and the injured thigh. Penicillin therapy was then stopped, but the urticaria persisted over a four week period. Patch tests and intradermal tests with penicillin elicited no reactions, there was no history of drug ingestion and no focus of infection could be found. The urticaria recurred with all severity one week later, and he was then referred for psychiatric investigation.

*Psychiatric History*—The patient was an intelligent, pleasant and cooperative officer. He was the fifth of seven children and had a happy, uneventful childhood.

14 Michelson, H. E. Psychosomatic Studies in Dermatology. The Motivation of Self-Induced Eruptions, *Arch Dermat & Syph* 51:245 (April) 1945.

life His mother was a mild, affectionate type, while his father was an aggressive, successful business man who "ruled the home" but was not tyrannical in nature The patient was an honor student until his third year in high school, at which time he began to associate with an older group of boys, drank excessively and took an inordinate interest in the opposite sex His schoolwork suffered correspondingly, and he failed to complete the grade successfully He was persuaded against his will to try the third year of high school the following year, but he again failed and was given a job starting "at the bottom" in his father's business He went ahead aggressively and worked his way up, and after eight years he was slowly buying out his father's share of the business There were no conflicts in the sexual sphere; he married at 20 years and had a happy domestic life

Further questioning disclosed that he always resented following orders blindly or submitting to authority per se His characteristic reaction to authority was always one of aggression His father intended that he should become a lawyer, and his schoolwork was modified accordingly (and against his wishes) in the third year of high school The failure to complete the school year may thus be explained as a hostile reaction to parental domination

His Army life was a series of conflicts with repeatedly successful aggressive solutions He entered as a draftee, soon became a corporal and attended schools in motor maintenance, with advancement in view When none was forthcoming he transferred to the air corps and did well as a cadet officer However, when his group was transferred to the infantry he controlled his bitter feelings, worked his way into officer's candidate school and graduated as a second lieutenant He had a severe conflict following orders blindly in the Army, developed great resentment and had great difficulty in controlling himself Executing "blind orders" invariably produced a feeling of oppression and inward resentment During the same period claustrophobia gradually developed This began as a feeling of discomfort in classrooms and barracks but slowly progressed to the point of acute anxiety and oppression on shipboard, in tanks or in foxholes

He was wounded on April 14, 1945, was evacuated, was given anesthesia and was put in a cast He awoke to find himself helpless, rigid and unable to move He was anxious and felt frustrated, "fenced in" and enraged These symptoms became increasingly severe during the next nine days, until finally severe generalized urticaria developed, which subsided gradually during a four week period A full hip and leg cast was applied one week later, and the body was immobilized from the waist down The feeling of claustrophobia became greatly intensified, and within an hour the urticaria returned with its original intensity At this time the patient was seen by a psychiatrist, and the possible relationship of the emotional factors (claustrophobia) and the cutaneous lesions was pointed out The eruption became less pronounced during the day and, after further reassurance, completely disappeared after another twenty-four hours

In summary, the patient was an overaggressive one in whom claustrophobia developed on being "fenced in" by military discipline Severe urticaria developed after he had been in a cast for nine days and had penicillin for a like period The initial reaction had features of developing sensitization to penicillin, but the return of the eruption five weeks later, after the patient was immobilized in a cast, indicated that the reaction had both a sensitization and a psychosomatic component

There are however certain disadvantages of this type of management The first, and probably the most important is its impracticability Many patients cannot afford the luxury of more than one physician

while others, unconvinced of the psychosomatic nature of their illness, refuse psychiatric consultation. Secondly, there are those who lose confidence in the dermatologist (because of his request for further consultation) and consequently lapse from observation, thus presenting a failure in treatment. Moreover, it is often difficult for a psychiatrist, uninitiated into the vagaries of dermatologic diagnosis, to correlate the presenting complaint in a chronologic fashion with the underlying etiologic factors. In these circumstances, a diagnosis of "no psychiatric disease" may be returned and the chance for cure permanently lost. Lastly, adequate diagnosis and therapy may be unobtainable because of divergences in personalities of the two physicians and in their approach to the problem. When such differences exist, the cooperation of a patient is quickly lost and failure of therapy becomes inevitable.

There are some cases, however, in which deep-seated, basic conflicts or gross psychiatric disorders of a serious nature are present. Little benefit can be expected in these cases by either the psychosomatic approach or the combined dermatologic and routine psychiatric care. In this group, fortunately, small, prolonged psychoanalysis, hypnoanalysis and free association or other specialized techniques are mandatory procedures. The failure of routine dermatologic-psychiatric therapy and the necessity for prolonged analysis are well illustrated by case 12.

**CASE 12**—A corporal aged 29 had been bothered with pruritus ani for the past six years. He was a lawyer in civilian life and did clerical work in a hospital during his two and one-half years of Army service. He had a strong mother fixation and, in consequence, showed almost no interest in the opposite sex. He never masturbated, and his few sexual experiences, exclusively with prostitutes, were prompted by infrequent bouts of drinking and erotic conversation with his drinking companions. He felt no drive toward the opposite sex and in general preferred male to female companionship. His father was easygoing, but his mother was an aggressive, dominating woman, who early in life impressed him with the importance of making professional attainments his goal, to the exclusion of recreation and "wasting his time with women."

His behavior was always compulsive in nature. He graduated from high school and then from college with a law degree and a year later with a master's degree. He supported himself during college and during his first year in law practice by working nights as a newspaper reporter, an average total of twelve to fourteen hours of work daily for some six years. Since being in the Army he held a routine clerical position, and frustrations over his inability to advance himself and conflicts with his superiors resulted in a notable increase in the frequency and severity of the pruritus.

The pruritus began while he was going to law school and grew slightly worse during his one and one-half years of law practice but was more frequent and severe during his army service, i. e., the period of greatest frustrations and of separation from his mother. The pruritus occurred in attacks lasting three to five minutes and appeared every two to three days. He described the attacks as beginning with a sensation of warmth around the anus, followed by sudden intense itching, which reached a climax after three or four minutes of violent excoriations and then rapidly disappeared. The tendency to pruritus had been relieved slightly

by symptomatic and roentgenologic therapy, while several interviews with the psychiatrist were followed by only moderate improvement

It is evident that the pruritus and in this case was an expression of frustration and a defense against inner conflict, both in the work and in the sexual sphere. Its pruritic nature was symbolic of resentment against the environment, its pattern indicated a masturbating component and relief of sexual tension, while its location was in a zone of sexual perversion and therefore symbolized his excessive mother needs and the subsequent latent homosexuality

Narcohypnosis is another method by which a patient with a psychosomatic dermatosis can be studied. This procedure is a convenient short cut and is of especial value in the management of acute disorders characterized by conscious block and in the confirmation of the dermatologic diagnosis in more chronic dermatoses. The advantages and limitations of narcohypnosis are shown in case 13

CASE 13—A private aged 39 presented for examination typical dermatitis factitia of the legs. The eruption began some four years previously and had been present intermittently to the date of hospitalization, with crops of new lesions appearing every three or four weeks. The lesions consisted of bizarre-shaped ulcers, frequently surmounted by hemorrhagic crusts and not surrounded by zones of erythema. The eruption was confined to the legs, with the longitudinal axis of individual lesions occurring in various planes. There was complete anesthesia to pain in the lower extremities. Involution was obtained by covering the involved areas with Unna's boots for ten days, but new ulcerations were present twenty-four hours after removal of the protective boots

*Psychiatric Investigation*—No information could be obtained by routine psychiatric consultation. The following data were elicited during several sessions of narcohypnosis with sodium amytal. The patient had an "unsatisfactory" home life (details not elicited) and ran away at the age of 16. At various times he had been a beggar, stowaway and in prison. He lived with a group of homosexuals for a year and had practiced homosexuality. He then married, but after his wife became pregnant he ran away and rejoined his friends. He enlisted in the Navy, was finally convicted of homosexual acts and was discharged. He was drafted into the Army, where he was extremely unhappy and maladjusted. He was a heavy drinker and on one occasion attempted suicide. He denied that he had produced the lesions intentionally but admitted that he had awakened on many occasions to find blood under his finger nails or on the bed clothes. The psychiatric diagnosis was psychopathic personality with hysteria

After the failure of routine psychiatric study, sufficient information was obtained in case 13 by narcohypnosis to establish a psychiatric background for the diagnosis of dermatitis factitia. Similar use was made of narcohypnosis in several other cases, in all of which a rough linkage between underlying maladjustments and the presenting condition could be made. Forman<sup>15</sup> has recently investigated 20 patients with excoriated or lichenified dermatitis, pruritus, urticaria and dermo-

15 Forman, L. Evipan Used in the Investigation of Some Chronic Dermatoses read at the Annual Meeting of the British Association of Dermatology and Syphilology, July 6-7, 1945

graphism, by the use of narcohypnosis with hexobarbitone. With the aid of this drug he was able to identify concealed anxiety states, excessive maternal attachment, depression, paranoid trends and evidence of hysteria. In the present series, however, narcohypnosis was of value mainly in patients with hysterical tendencies and conversion symptoms. Detailed psychosomatic studies were of greater usefulness in the majority of cases, for a more exact correlation between basic conflicts and the development of the presenting dermatosis could be obtained. Furthermore, narcohypnosis was found to have definite limitations in the field of therapy. Such transference as did occur between a patient and a psychiatrist was largely of a negative type, the patient actively resisting the attempts of the physician to deprive him of the dermatosomatic solution of his conflicts. Consequently, treatment with this modality was of limited value.

#### CORRELATION BETWEEN PSYCHOSOMATIC DERMATOSES AND PERSONALITY TYPES

The recent contribution of MacKenna<sup>7a</sup> has brought into sharp perspective the belief that the personality type may influence the form assumed by a neurodermatosis. The widely accepted view that hysterical persons are prone to mutilate their skin has been confirmed recently by a British group of investigators,<sup>1</sup> who found that 48 per cent of patients with factitial eruptions had a background of hysteria. Stokes and his associates,<sup>3a</sup> however, were the first to point out that certain dermatoses occurred commonly in patients with a relatively uniform personality configuration but in the absence of psychoneurosis or psychiatric disease. In their work on atopic eczema, later confirmed by the studies of Rogerson,<sup>3e</sup> Lynch and his co-workers<sup>11</sup> and others, they showed that the "atopic" person was a person of compulsive character—hostile, resentful, usually aggressive, egocentric, supersensitive, hyperactive and above average in intelligence. Likewise, the views of Stokes<sup>3a</sup> on rosacea have been substantiated by the work of Klaber and Wittkower.<sup>9</sup> Patients with rosacea were found to have conflicts in the social or sexual spheres, which, coupled with an abnormally high level of self esteem, led to anxiety and subsequent feelings of guilt and shame.

MacKenna, however, goes so far as to suggest that the personality types, which in exaggerated forms would constitute examples of psychoneuroses or psychopathic personalities, may be equated with more or less distinctive types of psychosomatic cutaneous disorders. In his opinion a hysterical person is subject to dermatitis factitia, a compulsive-obsessional person to diffuse prurigo, lichen simplex chronicus and pruritus ani, a person with severe anxiety to rosacea, seborrheic dermatitis, pompholyx and lichen planus and a borderline psychopathic personality (narcissism) to exudative dermatitis. His associates and

conferes<sup>1</sup> have made further studies along this line and in a general way have confirmed his beliefs, although much overlapping of symptoms and types has been noted. For example, of patients with neurodermatitis, 42 per cent had anxiety symptoms and 30 per cent evidence of hysteria. Forty-six per cent of the patients with seborrheic dermatitis showed anxiety and 35 per cent depression. Forty-eight per cent of those with dermatitis factitia had hysteria, but another 39 per cent showed gross anxiety, while 10 per cent manifested simple depression. Forman's studies<sup>1</sup> showed no significant correlation except that patients with anxiety manifested either lichenification or excoriated dermatitis. Wittkower's observations on patients with seborrheic dermatitis disclosed both anxiety and obsessional personality features, in general, conflicts were with authority, in the sexual sphere or with society as a whole. Attempts to identify a uniform personality type in patients with psoriasis were unsuccessful.

In an effort to confirm or disprove the contention of MacKenna, personality analyses were made in 40 cases of psychosomatic dermatoses and the types correlated with the presenting dermatosis. As would be expected, an imperfect correlation did exist, but the exceptions were so numerous as almost to disprove the rule. Dermatitis factitia was found in patients with anxiety neurosis, psychopathic personalities and various types of conversion hysteria. Pruritus occurred in all the main groupings. Neurotic excoriations constituted the only manifestation in which there was a constant association, namely, with severe anxiety. A more detailed psychosomatic study of individual cases was then made and the basic fallacy of personality studies became apparent. It was found that the presenting dermatosis depended not only on the personality type of a person in his life setting but also on the nature of the predisposing and precipitating stimuli. For example, a soldier with a long-standing tendency to neurasthenia had lichen simplex chronicus as a result of prolonged anxiety, but when a strong element of fear was added acute generalized urticaria supervened. Or, again, an officer of executive rank had an obsessive-compulsive type of personality. An oozing scrotal dermatitis developed after an unhappy love affair, a generalized pruritus appeared during periods of dissatisfaction with the entire environment, while urticaria and dermographism occurred when his concealed hostility (anger) became concentrated on insubordinate officers.

It would seem, therefore, that personality evaluations, while a useful adjunct in diagnosis and therapy, are grossly inadequate in the analysis of any given patient. They must be supplemented by other studies.

*The Psychosomatic Approach* A psychosomatic dermatosis is, by definition, one which contains both psychic and somatic elements. The psychosomatic study of a dermatosis embodies all that is best in routine dermatologic and psychiatric care. It first traces the psychic and physical

growth of a patient through his life span, influenced by the evolution of instinctive drives, on the one hand, and by the general pattern of his adjustments to his environment, on the other. A basic personality pattern is then constructed, and for adequate personality measurement dermatologists should familiarize themselves with the common types of psychoneuroses and psychopathic personalities. An excellent discussion of these conditions has been presented by Weiss and English.<sup>8</sup> With this information as a background, an attempt is made to correlate the onset and the development of the present illness with stresses, strains, traumatic events and conflicts. Somatic components in the dermatosis are then evaluated.

To facilitate the appraisal of the patient, the following psychosomatic history is submitted. It is a simplified condensation of the psychosomatic approach compiled by Dunbar,<sup>6</sup> modified by standard psychiatric methods and by personal trial and error studies over a period of years.

#### I Psychosomatic history

- A Brief description of presenting condition and initial impression of patient
- B Family history
  - 1 Parents marital history, personality types strictness
  - 2 Siblings number chronologic position of patient
  - 3 Nervous and mental status breakdowns psychoneurosis
  - 4 Allergy and other disease
- C Personal data
  - 1 Pseudohereditary tendencies (development of symptoms similar to those of parents)
  - 2 Death of parents in relation to age of patient
  - 3 Engagements, marriages, divorces
- D Health record
  - 1 Diseases reactions to interest in attitude to general physical status
  - 2 Addictions tobacco, alcohol drugs (need for)
  - 3 Injuries types and frequency of
  - 4 Dreams types and frequency of
  - 5 Neurotic traits early nail biting, thumb sucking bed wetting tantrums lying and stealing late fears, compulsions tensions
- E General adjustment (to self and to environment)
  - 1 Self body and personality
  - 2 Family infancy, childhood adolescence adult life
  - 3 School progress, interests
  - 4 Social playmates and friends religion hobbies
  - 5 Sex development adult pattern, necessity of normality of conflict to expression of, as escape mechanism (correlation with C3)
  - 6 Work necessity for, choice of, satisfaction with persistence in income
- F Behavior pattern
  - 1 Compulsive or spontaneous
  - 2 Dominating or submissive
  - 3 Goals pleasure ambition or altruism
  - 4 Emotion cheerful depressed unstable etc
  - 5 Introversion or extratension (motivating stimuli from within or without)
  - 6 Constricted or dilated (few or many interests)
  - 7 Reaction to authority (how are tension and conflict relieved?) (thinking talking out troubles substitute activities active aggression)
- G Preparation of patient for illness
  - 1 Correlation of prolonged conflicts and life situation prior to onset with type of person in his life setting as shown by B C D E and F
- H History of the present illness
  - 1 Chronologic correlation of stresses strains traumatic events and subsequent conflicts with appearance and progression of present condition
  - 2 Purpose served by symptoms
    - (a) Symptoms an expression of and defense against conflict
    - (b) The idea of compensation
    - (c) Escape from unpleasant duty
    - (d) Centering of attention on inadequate personality
  - 3 Will to get well
  - 4 Reactions to present illness
    - (a) Enjoyment, fear pain and discomfort of
  - 5 Amount of associated neuromuscular tension dreams
  - 6 Insight into present condition

The method of taking the history is of the greatest importance. At the onset, a routine dermatologic history already will have been obtained and some rapport with the patient established. For the psychosomatic history, however, information should never be forced from a patient by "hammer and tongs" questioning. It should be recalled that the dermatosis is the patient's defense against conflict. As such, he will be exceedingly loath to part with it unless some more normal outlet for the conflicts can be substituted. Accordingly, a physician should proceed with tact and guile, utilizing free association in casual conversation. For more details concerning the method, the reader should refer to Dunbar's "Psychosomatic Diagnoses" <sup>6</sup>

To illustrate the results which can be obtained with this technic, as compared with a routine history, cases 14 and 15 are presented.

*CASE 14—Routine History*—A private aged 26 was in the Army two and one-half years but was never in a combat unit. The past and family history were apparently irrelevant. Generalized pruritus had developed eighteen months previously, without obvious cause, and had persisted to the time of consultation. It was greatly aggravated by an attack of scabies four and one-half weeks previous to consultation. After one week therapy with sulfur was administered for three days, and the eruption improved but, because of persistence of itching, a two day course of benzyl benzoate was given. On examination there was no evidence of residual scabies, but there was a mild treatment dermatitis, with persistent itching which was out of proportion to the amount of residual dermatitis.

*Psychosomatic History*—The patient was the second youngest child in a family of seven. The mother was easygoing and affectionate, the patient was her favorite child. The father was dominating, excessively strict and intolerant of human foibles. The mother died of diabetes when the patient was 17. He married at 23 and had a reasonably happy home life with his wife.

*Health Record and General Adjustment*—He never had a serious illness. He was always a moderately heavy smoker and in civilian life drank somewhat excessively "to get away from the daily routine and for lack of something better to do." He fractured his left leg in January 1944. The only neurotic trait was nose picking for the past fifteen years.

He was always closely attached to his mother. This was resented by his father, who constantly abused him by his attitudes, actions and physical punishment. Following his mother's death he lived at home for three more years, but with constant friction with his father, for whom he lost all admiration because of a subsequent marriage. Despite this, he was emotionally disturbed by his father's lack of interest and love for him. He became temporarily out of work at the age of 20 and was ejected from home by his father. He then went to live with another family, with whom he assumed the role of a son, after two and one-half years he married the daughter of the family. The sexual life was normal in its development and in its adult pattern.

He was a high school graduate but never was particularly interested in school, with the exception of a vocational class in printing. He had no intellectual ambitions and left school, without regret, at the age of 15. He had worked intermittently at odd jobs since the age of 10 and more or less constantly since leaving school. He had never been greatly interested in his work and changed jobs eight times in seven and a half years. The best weekly wage had been

\$40, in general he averaged about \$20 per week. His social life was rather limited, he had many acquaintances but few friends. He had no hobbies, and his only outlets were drinking and "the movies."

*Behavior Pattern*—Behavior was spontaneous in nature. He lived in the present and for pleasure rather than long range ambitions or altruistic aims. Socially, he was submissive rather than dominating, he was shy and a relatively "poor mixer." The personality was constricted and extratensive. Emotionally he was unstable, but the predominant mood since being in the Army was one of depression. Reaction to authority was by submission, with avoidance of direct conflict. Tension was relieved in part by drinking, by talking out his troubles and by substitute activities such as the movies.

*Preparation of the Patient for Illness*—The events leading up to the present trouble were those of his two and one-half years of Army life. He was assigned to a noncombat baker's unit until he was transferred to the detachment of a convalescent hospital five months previous to consultation. He became a sergeant after three months but was reduced to a private two months later because of a minor infraction of rules. He regarded the demotion as an unjust discrimination and was considerably upset. He was soon reinstated as a sergeant but was again demoted, three months later, for overstaying a pass one-half hour. He was then court-martialed for the alleged theft of a pen.

*History of the Present Illness*—Generalized pruritus was first experienced during the court-martial proceedings. He was exonerated of the charge but harbored a great deal of unconscious resentment for his commanding officer. Three weeks later he jumped from the cab of a truck and fractured his right leg. It is possible, as Dunbar has shown<sup>6</sup> in similar instances, that the fracture was in effect an escape mechanism. Because of it, he was transferred from his unit, which was soon sent to a combat zone. In this connection it is important to mention that he had an immoderate fear of becoming a battle casualty and of not returning home to his wife.

Convalescence from the fracture lasted eight months, following which he was attached to the transportation department of the convalescent hospital. The pruritus continued during this period, during which he greatly resented the overbearing and domineering attitude of the transportation officer. However, the patient was careful to avoid actual clashes. The pruritus, indicative as it was of dissatisfaction with a hostile environment, soon proved to be ineffective as a defense against conflict. He became shaky and had a "drawing feeling in his stomach," and pains developed in the occipital region of the scalp and over the crest of the left ilium. Overt anxiety appeared in the month prior to the present hospitalization, and he complained of nosebleeds from the right nostril, the one traumatized mostly by picking.

The pruritus was much aggravated by a recent attack of scabies, persisted after thorough sulfur treatment and prompted a course of benzyl benzoate, which in turn caused a treatment dermatitis. On admission no evidence of scabies was found, and the treatment dermatitis cleared promptly with a soothing regimen. The pruritus, on the contrary, persisted unabated. There was some relief and some pleasure derived from excoriation, which, however, was never prolonged and was not suggestive of cutaneous masturbation. He had no insight into the nature of his illness.

*Summary*—The patient was a passive, submissive and somewhat depressed person. He always needed some one to protect him but never achieved this need in military life. His characteristic reaction to authority was one of avoidance. The essential causative factor was a detached, unsympathetic domination in a person who

actually required domination of a sympathetic, benevolent and protective type. Adequate outlets to his emotional tension were not available. His escape mechanisms were (1) generalized pruritus, (2) fracture, (3) somatic expressions of anxiety and (4) recent development of overt anxiety. The pruritus was explained as a conversion phenomenon, an expression of conflict through a somatic outlet which avoided authority, and was to some extent pleasurable. This response was in keeping with his personality and with previous adjustments to difficult situations.

**CASF 15**—A private aged 23 had severe hyperhidrosis and symmetric erythema of the feet and excessive perspiration of hands, axillas and genital region for some ten months. Routine questioning did not disclose an obvious cause for the syndrome.

**Psychosomatic History**—**Family History and Personal Data** The patient had one brother seven years his senior. A sister died when he was 7, at which time his mother had a severe nervous breakdown and subsequently deserted the family. She had always been emotionally unstable, while the father, with whom the patient was brought up, was easygoing in nature.

**Health Record and General Adjustment**—The patient had never been seriously ill. He had taken alcohol excessively since the age of 16, but more so since being in the Army. Drinking was an escape from the troubles of life, the main incentive of late being a dissatisfaction with Army life and lonesomeness for home. Dreams were frequent and were concerned mainly with returning home or with home scenes. He was a nail biter, while bed wetting had occurred until the age of 6. The general adjustment was good. He got along well with people, but largely in a negative way, since he was diffident and retiring in nature. He had no particular scholastic ambitions and left school to work on his father's farm on completing the sixth grade. He was contented with farm life and had no desire to own a farm or otherwise better his station in life. There were no conflicts in the sexual sphere.

**Behavior Pattern**—Behavior was spontaneous rather than compulsive, while the personality was constricted and extratensive. He was not ambitious or an especially hard worker and was still a private after nearly three years of Army life. The predominant mood since being in the army was one of depression. The reaction to authority was one of docile submission, and obvious conflicts were not precipitated by domination by his superiors.

**Preparation of Patient for Illness**—Hyperhidrosis, either local or general, had never been present in civilian life or during Army service prior to entering combat, despite strenuous labor in a warm climate. He entered combat June 10, 1944, and within a few days he became nervous, shaky and jumpy. These symptoms became progressively severe until he was evacuated to the United Kingdom on July 7 because of a minor shrapnel wound in the left thigh.

**History of Present Illness**—Hyperhidrosis of the feet was first noted three weeks after beginning combat duty. It rapidly became worse and was soon accompanied with symmetric erythema limited to the soles and sides of the feet and by actual hemorrhages from the eroded areas. The feet became sore and painful, and symptoms of flat feet developed. Despite hospitalization, the process continued unabated and kept him in the hospital for four months, long after the wound had healed. After temporary improvement he was sent to the replacement center and began infantry training prior to reshipment to a combat unit. The hyperhidrosis and erythema soon recurred with their original severity. Simultaneously, and for the first time in his life, he noted severe hyperhidrosis involving the axillas, hands

and genital regions. He was then placed on noncombat duty in the United Kingdom. During the six months prior to hospitalization, there was only slight improvement in the hyperhidrotic state and he was still troubled by mild symptoms of free-floating anxiety. He was somewhat pessimistic regarding cure and had no insight as to the cause of the present illness.

*Summary*—The patient was a submissive, somewhat depressed soldier who lacked the instinctive drive, ideologic stimuli or sense of group companionship which would enable him to partake successfully in active combat. Confronted with actual combat anxiety symptoms, severe hyperhidrosis and symmetric erythema of the feet developed. Literally, his feet "bled" for him to be removed from combat. A later preparation for combat again called forth a beginning fear reaction, and the return of the disorder of the feet was accompanied with a more general type of hyperhidrosis. It may be observed that what began as a purely psychogenic hyperhidrosis eventually assumed a fixed somatic pattern, persisting long after the removal of the precipitating conflict. Prolonged psychotherapy supplemented by roentgenologic treatment and other symptomatic measures will probably be necessary to effect a permanent cure.

In conclusion, it will be seen that the psychosomatic approach has many advantages over other methods of investigation. It requires only a moderate amount of experience and a liberal dash of common sense and can be obtained in from one to three hours. Moreover, it lends itself well to the management of all but the more long-standing, recalcitrant conditions, for which prolonged psychoanalysis is indicated. Lastly, a patient is under the guidance of a single physician. As such, continued doses of psychotherapy can be administered and environmental adjustments made while roentgenologic and other symptomatic methods of treatment are being given.

#### SUMMARY

- 1 Basic conceptions of psychosomatic dermatoses have been presented.

- 2 An analysis of various methods of investigation of the patient with a neurodermatosis has been made.

- 3 A psychosomatic approach to the study of neurodermatoses is submitted.

66 East Sixty-Sixth Street

## ACARODERMATITIS URTICARIOIDES

I KATZENELLENBOGEN, M D

JERUSALEM, PALESTINE

IN PALESTINE the existence of many cutaneous diseases causing itching and a rash—urticaria phlebotomica, scabies and miliaria rubra—has obviously overshadowed the rather modest but nevertheless important acarodermatitis urticarioides, which is caused by the mite *Pediculoides ventricosus*.

In 1937 I<sup>1</sup> described a rash found among milkers, which was traced to the handling of hay coming from a communal settlement near Haifa. *Pediculoides ventricosus* was suspected to be the causative agent. On examination numerous dead insects and insect larvae of the lepidoptera and coleoptera types were found, but no *Pediculoides ventricosus* mites could be traced. Every year since 1935 I have seen single and group cases. In 80 cases investigations were made to find the origin of this rash. In 1944 I succeeded in finding *Pediculoides ventricosus*, and this enables me to report on the epidemiology of this disease in Palestine. Farmers, porters, drivers, milkers and stablehands were among the persons affected.

### TYPES OF INFESTATION

*Direct Infestation*—J K, in May 1936, complained of a severe itching on the back for five days. The patient presented an urticarial type of eruption on the back and the upper parts of the arms. The right side was more involved than the left. The individual lesions were discrete papules, many of them surmounted by a tiny central vesicle of pinhead size, filled with a clear fluid. No signs of a secondary infection were noted. An investigation revealed that the woman had been sleeping for several nights on a straw mattress which had been stored in a cellar for six months. The patient admitted that she usually slept on the right side.

Straw mattresses were responsible for the appearance of a similar rash in 8 other cases. In 1 case the eruption was followed by a rise in temperature and a swelling of the axillary and the inguinal glands. The severe itching and the vesicles surmounting the urticarial rash aided in the diagnosis. Ten days after the straw mattress had been removed the eruption disappeared and the woman recovered.

Another woman, who slept for one night only on the same mattress, had a similar but milder eruption and no general symptoms of illness.

From the Skin Department of the Bicur Holim Hospital and the Outpatient Department of Kupat Holim.

1 Katzenellenbogen, I. Die Berufskrankheiten der Melker in Palästina, Harefuah **12** 1-111 (Feb) 1937.

*Indirect Infestation*—Eruptions were noted even when contact with the infested grass or grain was indirect. During October 1939 5 workers from a soda water factory reported with the typical rash on the neck and the shoulders. In no case was the skin under the belt affected. The workers were not living in common quarters, and it was obvious that the pathogenic material ought to be found in the rooms of the factory. An investigation disclosed that two sacks with grain were brought in September to the factory and stored next to the place where the workers used to put their coats or shirts during working hours. As the garments were in direct contact with the sacks, dust and parts of the grain covered the inside of them.



*A*, acarodermatitis urticarioides due to sleeping on an infested straw mattress. The patient slept on the right side, *B*, acarodermatitis urticarioides and chickenpox simultaneously in 1 patient.

*Infestation During the Winter*—In December 1942 the personnel of a workers' mess near the Dead Sea were affected by a severe itching eruption. An intense irritation of the neck, shoulders and forearms was noted. In a woman the occipital part of the scalp was involved. The tiny papules were surmounted by vesicles. Sardines had been eaten on the day prior to the eruption and were suspected by the patient of being the source of the rash. Visitors to this restaurant who also ate sardines showed no signs of an eruption.

An investigation revealed that on the previous day sacks and boxes containing eggs packed in straw had been brought into the storerooms.

of the establishment. The driver who carried the sacks and who helped to unload them had a similar eruption. A short time after the straw was destroyed the eruptions of the affected persons disappeared. The straw was brought to Jerusalem for examination. *Pediculoides ventricosus* was not found.

In all previously recorded cases the suspected straw, grass or grain was sent to a laboratory for examination, which often took weeks. The mites, however, were easily found when in July 1944 grass was examined immediately after being suspected of harboring them.

#### REPORT OF A CASE

A truck driver, 30 years old, one day had to transport bales of grass from the railway station to cow barns in a suburb of Jerusalem. Together with a few laborers he helped to unload the bales and noticed numerous dead black insects in the grass and a greenish dust on the bottom of the truck after it was unloaded. The same night an intense irritation started, and the severe itching and rash brought him to consult me twelve hours later. An examination showed discrete papular lesions, ranging from the size of a lentil to that of a bean, with urticarial wheals partly surmounted by tiny vesicles. They covered the skin of the chest, the neck and parts of the groins. Only a few lesions appeared on the back. The intense irritation became worse during the next three days and nights. The patient could not sleep in spite of antipruritic treatment. Then the itching subsided, and the lesions flattened. After seven more days reddish brown irregular excoriations were seen, and after another five days the rash completely disappeared. In all the cases observed the eruption had an exanthematous character. The lesions were of the urticarial type and nearly all of the same size. They were discrete and often surmounted by tiny vesicles. After a few days the urticarial character subsided and the rash had now a rather macular appearance. There were erosions after scratching but no signs of secondary infection. The tiny vesicles previously regarded as obligatory were absent in the following cases.

*Histologic Examination* (made by Prof. E. E. Franco).—A biopsy was performed twelve hours after the appearance of the rash. The excised skin was fixed in Zenker's fluid. There was a circumscribed elevation of the thinned epidermis, with parakeratosis in a few fields. In the malpighian layer the prickle cell layer was poorly developed, the papillary body was flattened and there was a striking diminution of the interpapillary processes. Considerable hypertrophy of the stratum granulosum was seen. There was a diminution of the pigment cells in the basal layer, and the basal cells were poorly pigmented. In the derma, a moderate infiltration with lymphocytes around the vessels was present. There were no chromatophores and no signs of acarids in the skin.

#### EPIDEMIOLOGIC REPORT

All workers in cowsheds to which grass suspected of having mites was delivered were examined. An investigation was carried out in the settlement in Haifa Bay from which the bales had been sent. An entomologic examination of the suspected grass was made. Fourteen workers handled the grass, which was delivered by truck. All of them suffered from a highly pruritic eruption. Four workers who helped the driver

to unload the bales were affected during the same night. Those were the patients with severe eruptions. The 10 other workers had to handle the grass for a few minutes daily. They lifted the bales on their forearms and brought them on their shoulders to the cows.

The localization of the eruption, the density of the lesions and the ferocity of the itching depended on (a) the extent of contact of the skin with the grass and (b) the frequency and the duration of this contact. One worker, who was dressed in overalls while handling the grass, felt the itch on the back and the upper part of the shoulder only. Another, who was dressed in shorts and a vest and who helped for several hours with the bales, suffered from a dense rash over practically the whole body. The size of the lesions was not greater than in the previous case, although more vesicles surmounted the wheals. The eruption was particularly dense on the forearms and the shoulders. The lesions, though extremely dense, remained discrete.

*Duration of the Rash*—The eruption lasted from eight to ten days, during which time further contact with the infected grass was avoided.

The proprietor of the barn handled the bales only once, for ten minutes. A rash developed on the same day and disappeared nine days later. In the case of the truck driver who had contact with the grass only once but for a prolonged period, the rash disappeared after thirteen days although the severe itching subsided after three days. Five workers continued handling the bales of grass for three weeks in spite of the itching and the rash. They then refused further work. Finally the workers came to an agreement. Every man handled the grass only once a week, dressed in overalls and wearing a gas mask. The rash subsided eventually, without leaving any pigmentation on the skin.

Every man who handled the grass, without exception, acquired the rash. No rise in temperature, asthma, cough or other constitutional effects were observed among the patients affected.

#### EXPERIMENTAL STUDIES

In my presence 4 workers lifted the bales on their forearms and transferred them from one place to another. Contact between the skin and the grass lasted for two or three minutes. Five minutes later pale, highly irritating wheals appeared on the forearms. A few minutes later the pallor disappeared, and a bright erythema became visible. When the same experiment was performed six weeks later with the same grass, no reaction was observed.

*Investigation in the Field* At Nirhaim in Haifa Bay, from where the grass was sent to Jerusalem, the local physician traced 12 persons affected by the same rash. All of them handled dry grass. The disease was known to the farmers, but they seldom approached a physician.

for treatment of it Dr Rivnai,<sup>2</sup> of the Agricultural Experimental Institute, gave valuable information about the grass in question at Emek Jesreel and Haifa Bay There are three varieties of grass, but only *fahleh*, a grass dried in the field, was responsible for the rash *Fahleh* is harvested several times a year, but it is only at the end of spring that the grass, after being harvested, is made into sheaves, pressed and left to dry in the field

It was found by the farmers that it was not the green grass but the dry grass left for weeks or months to dry in the field which caused the itch

*Fahleh* is used as a dry food for cattle and to a lesser extent for packing eggs, fruit and other products The producers send the grass directly from the field to the consumer

Dr Rivnai expressed the belief that *fahleh* is responsible for the itch in many other places in Palestine

In communal settlements the farmers have found a way out by limiting contact with the grass to no more than once a week

*Examination of the Grass for Mites* Grass or dust of the grass was put in a Petri dish With a binocular microscope quickly moving mites were easily discovered They were recognized as *Pediculoides ventricosus* by the entomologist This examination was repeated many times During the time when new rashes appeared, mites were always traced

The disappearance of the mites in the grass (as established by microscopic examination) coincided with the disappearance of new cases of this itch

#### COMMENT

The different names given to acarodermatitis correspond to the various sources of infestation with mites Some of the names are straw mattress disease, barley itch, cottonseed dermatitis and hay itch

Schamberg,<sup>3</sup> in Philadelphia, described an eruption which appeared every year during the months of May and June and occurred in persons who came in touch with straw from a certain locality Only eight years later Schamberg and Goldberger<sup>3</sup> succeeded in tracing *Pediculoides ventricosus* to straw mattresses In Italy acarodermatitis was often seen and described Majocchi<sup>4</sup> (1921) reported on 140 prisoners in the Bologna prison in Italy who suffered from the rash after spending a

2 Rivnai, I Personal communication to the author

3 Goldberger, J, and Schamberg, J F Epidemic of an Urticarioid Dermatitis Due to a Small Mite (*Pediculoides Ventricosus*) in the Straw of Mattresses, Pub Health Rep **24** 973-975 (July 9) 1909

4 Majocchi, D Sulla continuazione della epidemia di acariasi da grano nella provincia e città di Bologna, e di una epidemia circoscritta nelle carceri della stessa città (Nota clinico-statistica), Gior ital d mal ven **63** 124-127, 1922.

night on newly filled straw mattresses. Lou and Legangneux<sup>5</sup> (1919), described an epidemic eruption among dockers at Le Havre, France, during the years 1911 to 1919 which resulted from their handling grain arriving from the Levant. Rogers<sup>6</sup> recently (1943) described cases of grain itch among men handling bales of hay at Phoenix, Ariz. Levi<sup>7</sup> (1926) reported an epidemic among grain handlers at Trieste, Italy. He considered the resulting eruption as an accident and hence believed the patients were entitled to compensation. Schwartz and Tulipan<sup>8</sup> (1939) regarded acarodermatitis as an occupational cutaneous disease. Nixon<sup>9</sup> (1944), reporting about cargoes causing itch in reference to workmen's compensation, discussed the question of whether the eruption could be regarded as one scheduled as dermatitis produced by dust or liquids or as an accident at work.

Besides the cases in which the rash appears after direct contact with the offending material, other cases are reported in which the rash appears through indirect contact with dust containing the mites. Askins<sup>10</sup> (1924) reported the occurrence of a rash among dock laborers engaged in unloading barley from Morocco. The captain and the mate of the boat were affected, although they had not actually handled the barley. In another port the inhabitants of some cottages close to the dock where Moroccan barley was being unloaded acquired the disease, although not from contact with the grain. Thompson<sup>11</sup> (1925) reported an outbreak of "barley itch" through grain dust. A mechanical elevator was introduced, as men absolutely refused to handle the grain. "This made much dust, which was blown into some cottages near and infected all the women and children at home at the time." Courcelle and Molle<sup>12</sup> (1910) reported that one of them was contaminated through garments suspended close to samples of grain in his laboratory.

5. Lou and Legangneux. *Maladie cutanée provoquée par un pediculioïde trouvé dans un chargement d'orge arrivant au Havre*, Bull. Acad. de med., Paris **82** 308-310, 1919, cited by Girod.

6. Rogers, G. K. Grain Itch, J. A. M. A **123** 887-889 (Dec. 4) 1943.

7. Levi, I. Sopra la dermatite pruriginosa prodotta dall'acaro "pediculoides ventricosus" manifestatasi in forma epidemica tra gli scaricatori di orzo e di semi di lino nel porto di Trieste, Arch. ital. di dermat., **2** 110-130 (Dec.) 1926.

8. Schwartz, L., and Tulipan, L. A Text Book of Occupational Diseases of the Skin, Philadelphia, Lea & Febiger, 1939, p. 461.

9. Nixon, J. A. Cheese Itch and "Itchy Cargoes" in Reference to Workmen's Compensation, Proc. Roy. Soc. Med. **37** 405 (June) 1944, Brit. J. Dermat. **56** 235 (Nov-Dec.) 1944.

10. Askins, R. A. Dermatitis Caused by Pediculoides Ventricosus, Brit. M. J. **2** 950 (Nov. 22) 1924.

11. Thompson, A. G. G. Barley Itch, Brit. M. J. **1** 71 (Jan. 10) 1925.

12. Courcelle and Molle, cited by Girod, F. J. L. Le pediculoides ventricosus, Thesis, Université d'Algiers, 1936, no. 11.

*Time of Appearance* In Palestine acarodermatitis appears in June and July and in September and October. Around the Dead Sea, with its exceptional climatic conditions, an outbreak was recorded in December.

The epidemic becomes more widespread when favorable conditions for breeding exist. A temperature between 70 and 80 F and a humidity of 80 per cent are regarded as most favorable for multiplication.

*Differential Diagnosis* The eruption must be differentiated from urticaria, scabies, urticaria phlebotomica, other mite rashes and chickenpox. In urticaria the lesions disappear quickly, in acarodermatitis urticarioides they remain for seven to ten days, even if they change their appearance. By the characteristic distribution, the prevalence of the lesions on the private parts, the furrows and the finding of the Sarcoptes, one can easily differentiate scabies from acarodermatitis. The lesions of urticaria phlebotomica are usually limited to the arms and the legs. The lesions vary much in size. The malleolar region is practically always affected.

*Triombidiosis* The larvae of *Leptus autumnalis* live on grasses and shrubs and on the ground near vegetation. The cutaneous lesions produced are commonly on the ankles and the legs. The larvae may sometimes be seen in the center of the papules as red points.

Goats' itch and similar itches are produced by the tyroglyphidae present in cheese, copra and dried fruit. The lesions are similar to those of grain itch, and therefore entomologic examination is of great importance in establishing the diagnosis.

Acarodermatitis may resemble chickenpox and diagnosis may sometimes present difficulties, as in the following case.

R. B., a 9 year old girl, was first seen in August 1944, with a temperature of 40 C (104 F) and an eruption consisting of small red papules and vesicles, with the characteristic central sinking of varicella vesicles. Lesions were also noted on the buccal mucous membrane. While the rest of the body presented a moderate number of discrete vesicles, the back from the neck to the rubber belt of the garter was covered with copious small uniform papules, each capped by a vesicle. Under the belt on the buttocks the number of lesions was small, and all of them had the characteristic appearance of chickenpox (see B of figure). The skin on the back of the arms was more profusely attacked. The history of the case revealed that the girl was sent to a farm when her sister contracted chickenpox. The girl admitted spending a few hours lying in a grove on old wet straw, clothed only in a pair of knickers. The back and the upper parts of the arms were in close contact with the wet straw. On the following night a severely pruritic dense eruption appeared on the back. The next morning fever set in, and a moderate number of vesicles appeared on the rest of the body. While the dense eruption on the back disappeared after ten days, the vesicles of varicella persisted for fifteen days. Acarodermatitis and chickenpox simultaneously occurred in this patient.

*Complications*—In some cases acarodermatitis was reported to be followed by a rise in temperature, headache and nausea

Webster<sup>13</sup> observed acarodermatitis urticarioides accompanied in cases of severe eruption with general systemic symptoms, such as a rise of temperature from 99 to 110 F, general pains in the joints and backache. Puntomi-Pantaleoni<sup>14</sup> described a slight rise of temperature, lasting for one or two days. I noticed a rise of temperature only twice among 80 cases.

Ancona,<sup>15</sup> Frugoni<sup>16</sup> and Grove<sup>17</sup> discussed a peculiar form of asthma, which they attributed to the inhalation of dust containing acarids. This was not confirmed by Ciarocchi<sup>18</sup> and others. With the exception of an occasional cough I noticed no cases of asthma or throat trouble among my patients.

*Examination of the Blood* Schamberg<sup>3</sup> and Rawles<sup>19</sup> described leukocytosis and eosinophilia (8 to 12 per cent) in their cases. No pathologic changes in the blood were noted in my cases.

*Preventive Measures*—Chandler<sup>20</sup> suggested greasing the body, followed by a change of clothing and a bath after work. Riley and Johannsen<sup>21</sup> advised putting sulfur powder in the clothes and on the body. Roger's patients, on their own initiative, sprayed themselves with Shell Oil Fly spray (a product of the Shell Oil Company, Inc., consisting of a pyrethrum extract and highly refined kerosene) and claimed immunity from the bites of the mites.<sup>6</sup>

The best preventive method, however, seems to be the disinfection of straw, grass or grain. Loir and Legangneux<sup>5</sup> disinfested the shipload at Le Havre by burning sulfur (34 Gm to 1 cubic meter). The

13 Webster, F. M., cited by Hase, A. Zur pathologisch-parasitologischen und epidemiologisch-hygienischen Bedeutung der Milben, insbesondere der Tyroglyphinae (Kasemilben), sowie über den sogenannten "Milbenkase," Ztschr. f. Parasitenk. **1** 765-821 (March 26) 1929.

14 Puntomi-Pantaleoni, cited by Girod.<sup>12</sup>

15 Ancona, G. Asma epidemico da pediculoides ventricosus, Policlínico (sez. med.) **30** 45-70 (Feb.) 1923.

16 Frugoni, C., and Ancona, G. Ulteriori studi sull' asma bronchiale, Riforma med. **41** 409-415, 1925.

17 Grove, E. F. Studies in Specific Hypersensitiveness. Asthma and Dermatitis Due to Hypersensitiveness to Pediculoides ventricosus, J. Immunol. **12** 263-271 (Oct.) 1926.

18 Ciarocchi, L. Scabbia dei droghieri ed acariasi da cereali: insolito reperto di acari, Considerazioni sull' importanza dei processi allergici nella genesi delle manifestazioni cutanee da acari, Arch. ital. di dermat., sif. **5** 566-585 (May) 1930.

19 Rawles, L. T. Grain Itch, J. Indiana M. A. **3** 351-354, 1910.

20 Chandler, A. C. Animal Parasites and Human Disease, New York, John Wiley & Sons, Inc., 1918, pp. 337-339.

21 Riley and Johannsen, quoted by Chandler.<sup>20</sup>

grass was subjected to fumigation for ten hours. After ten hours no new cases of acarodermatitis occurred. In Palestine ethylene dibromide was found by Dr. Rivnai<sup>2</sup> of the Agricultural Experimental Station, to be the best agent for destroying the mites. The sheaves were piled and covered with a tent cloth, 25 cc of ethylene dibromide fluid was used for 1 cubic meter. Three to four days were required to destroy all mites.

#### SUMMARY AND CONCLUSIONS

An endemic eruption due to the mite *Pediculoides ventricosus* was observed in Palestine. The mites were found in straw and grass, with the latter being the main source of the infestation.

The forearms, neck and trunk were the parts most frequently affected, the legs scarcely and only when the grass came into direct contact with the skin. The lesions appeared first as pale, irritating nettle stings and later as a dense but discrete papulourticarial rash. In many cases central vesicles surmounting urticarial spots were noticed. The eruption lasted from six to ten days, during which time further contact with the infested grass or straw was avoided.

Acarodermatitis is endemic in Palestine. It appears in June and July and September and October. *Fahleh* grass dried in the field and sold mostly to owners of cattle all over the country was responsible for an outbreak of the rash among workers in cow barns in Jerusalem and in Haifa Bay. No constitutional effects were seen among the patients affected.

A case of acarodermatitis combined with chickenpox was observed in Palestine. Besides causing severe itching and insomnia, the eruption often meant a material loss in addition, since the laborers in town refused to handle the grass after the first appearance of the itch.

Fumigation with ethylene dibromide was found to be effective in destroying the mites.

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## TOPICAL USE OF PENICILLIN IN TREATMENT OF PYODERMA

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PRIMARY and secondary pyogenic infections of the skin make up a large proportion of dermatologic conditions in patients in the military services. In the hot and more tropical areas this group assumes increasing importance and comprises a constant problem.

The amazing effectiveness of penicillin on some of the pyogenic organisms would warrant a trial in purulent infections of the skin in which the process could be subjected directly to penicillin. Penicillin has been incorporated into water-miscible bases in varying concentrations. Cohen and Pfaff<sup>1</sup> used 1,666 units of penicillin per gram, with effectiveness, in impetigo contagiosa, carbuncles, herpes zoster with secondary impetigo and sycosis barbae. Johnson<sup>2</sup> reported excellent results in the same type of cases using a concentration of 166 units per gram of ointment base.

Vesicular and intertriginous fungous infections of the feet having secondary invasion by staphylococci and streptococci constitute a large group of conditions in patients admitted to military hospitals. This group of patients was routinely cleansed on admission and each subsequent day with soaks of 1:9,000 potassium permanganate solution along with débridement of necrotic tissue and localized pustules. The cases were roughly subdivided into three groups. In the first, 5 per cent sulfadiazine in a water-soluble ointment base was applied as a fixed dressing overnight, in the second, penicillin ointment in a concentration of 800 units per gram of water-soluble emulsion base was likewise applied as a fixed dressing, and, in the third, a thin dressing of old linen and gauze saturated with isotonic solution of sodium chloride containing 800 units of penicillin per cubic centimeter was followed by the enclosure of the involved part in a Bunyan bag overnight to prevent evaporation. The wet dressings of penicillin were removed each morning and the part allowed to dry in order to prevent excessive epidermal maceration.

The results were striking. The group having wet dressings of penicillin was by far the most improved. There were less exudate on

1 Cohen, T. M., and Pfaff, R. O. Penicillin in Dermatologic Therapy. Report of Results in One Hundred Cases, *Arch Dermat & Syph* 51:172-177 (March) 1945.

2 Johnson, H. M. Penicillin Ointment for Pyodermas, to be published.

the bandage, a diminution of the surrounding cellulitis and swelling and a pronounced decrease in pain and discomfort. The group treated with penicillin ointment usually improved more rapidly than those having the sulfadiazine preparation, but the infections of those treated with wet dressings of penicillin subsided more rapidly than that of those having either ointment preparation. The inflammatory process usually subsided within three to four days, leaving an irregular, partially desquamated dry area. The topical application of penicillin ointment once or twice daily was particularly effective at this stage in preventing cracking of the skin and in controlling recurrent areas of low grade infection.

In instances of extensive cellulitis accompanied with lymphangitis and moderate or severe degrees of lymphadenitis, supplementary intramuscular penicillin therapy in the usual doses of 25,000 units each three hours was effective in controlling the spread of the infection. Systemic penicillin therapy is seldom necessary for more than two or three days.

#### COMPLICATIONS OF TOPICAL PENICILLIN THERAPY

A fine papular erythematous dermatitis with intense itching occurs in about 40 per cent of the patients having wet penicillin dressings for five to six consecutive days. This seldom occurs before the fourth day. If therapy is omitted for one or two days, treatment can usually be resumed for two to three day periods without the occurrence of a contact dermatitis. When intramuscular penicillin therapy is being given simultaneously, it can usually be continued, or initiated, if indicated, without effect on the area of local dermatitis which subsides after the external contactant has been removed. Occasionally a similar erythematous reaction occurs after penicillin ointment has been used continuously for six to ten days.

Cohen and Pfaff<sup>1</sup> found 0.95 per cent of 524 hospitalized patients sensitive to penicillin ointment when patch tests were made. This number is exceedingly low when compared with the great number which demonstrate cutaneous reactions to wet dressings of penicillin in isotonic solution of sodium chloride after a period of four or five days' use. An acquired cutaneous sensitivity to penicillin solutions is not an uncommon observation in the personnel assigned to administering the injections in a large Army hospital. The dermatitis in this instance usually involves the hands or face, occurring in some after several weeks of exposure and in others after several months, and takes the form of diffuse erythema with scattered erythematous papules or small vesicles along with a mild to moderate subcutaneous edema.

Even though a contact dermatitis is not an uncommon complication after prolonged exposure of the skin to penicillin in solution, the results have been found superior to the ointment preparations. Greasy vehicles containing bactericidal agents are frequently unsatisfactory in controlling

purulent cutaneous infections. Ointments prohibit drainage, limit the penetration of the therapeutic agent into the deeper portions of the inflammatory process and favor the growth of facultative anaerobic organisms. The water-miscible bases decrease these hazards to some extent but do not completely eliminate them.

#### SUMMARY

1 The topical use of penicillin incorporated in water-miscible bases and in isotonic solution of sodium chloride as wet dressings has been used over a nine month period in an Army general hospital in the treatment of pyodermas.

2 Penicillin used in isotonic solution of sodium chloride at a concentration of 800 units per cubic centimeter is far superior to ointment preparations and amazingly effective in controlling cutaneous pyogenic infections.

3 Contact dermatitis is not infrequent after four to five consecutive days of use of wet dressings or six to ten days of ointment therapy.

4 This complication of contact dermatitis is minimized by the discontinuing of topical penicillin therapy for one or two days after four days of use of wet dressings or six days of application of ointment.

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## HYPERKERATOSIS PENÈTRANS

Report of a Case of a Probable Variant of Kyrle's Disease

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JOSEF KYRLE<sup>1</sup> described in 1916, from Finger's clinic in Vienna, the first reported instance of a disease to which he gave the name hyperkeratosis follicularis et parafollicularis in cutem penetrans. The patient was a 22 year old woman with an eruption of eight months' duration, characterized by polycyclic hyperkeratotic plaques in the axillas, on the forearms and on the shoulders. On removal of the heavy scale and crust, the plaques were seen to be composed of closely set, discrete, crateriform papules a few millimeters in diameter, topped by a central depression about 2 mm in width and depth. Microscopically, the floors of these depressions were seen to be formed by the bases of keratinous conical pegs, the points of which extended downward through the acanthotic epidermis and, in some of the papules, actually penetrated through the basal layer and entered the corium, where they excited a typical foreign body reaction. Kyrle considered the possible diagnoses of lichen ruber acuminatus, keratosis follicularis (Darier), lichen verrucosus, pityriasis rubra pilaris, keratosis follicularis contagiosa (Brooke) and follicular psoriasis but concluded that the disease was an entity *suu generis*.

Fried<sup>2</sup> in 1923 reported a second case, of one year's duration, that of a 61 year old cabinet maker, the eruption was more extensive and severer than that in Kyrle's case, with seborrheic features, only the palms and soles were wholly spared, all the nails were elevated by subungual keratoses, and the penetration of the epidermis by the horny plugs was less regularly observed than in Kyrle's patient. Diagnoses of psoriasis, lichen planus, keratosis follicularis, acanthosis nigricans and eczema folliculare hyperkeratoticum were considered but ruled out. Local treatment and injections of sodium cacodylate were without avail. Fried concurred in Kyrle's opinion that the penetration of the epidermis was accomplished not merely by mechanical action but by the action of the same damaging factor that produced the horny pegs in the first place.

1 Kyrle, J. Ueber einen ungewöhnlichen Fall um universallen follikularer und parafollikularer Hyperkeratose (hyperkeratosis follicularis et parafollicularis in cutem penetrans), Arch f Dermat u Syph **123** 466, 1916.

2 Fried, A. Ueber ein Fall von hyperkeratosis follicularis et parafollicularis in cutem penetrans (Kyrle), Arch f Dermat u Syph **143** 45, 1923.

Pawloff<sup>3</sup> in 1926 reported the third case<sup>1</sup>, in it the eruption occurred on the extremities and the right flank only. He described five varieties of lesions: gooseflesh-like follicular papules of pinhead size, with hard keratinous central plugs, grouped on the arms; bluish red papules with central craters and horny plugs, in half palm-sized groups, on the thighs; flattened hemispherical papules on the left forearm, without follicular openings; dirty gray rhomboidal keratotic plaques on the dorsa of the feet, traversed by deep clefts; and ichthyotic plaques on the legs and shins, with comedo-like plugs. He considered in the differential diagnosis the following diseases: lichen planus, lichen ruber acuminatus, keratosis follicularis contagiosa (Brooke) and keratosis follicularis. The histologic features, which were exactly like those described by Kyrle, led him to conclude that his case was an example of the same disease that Kyrle had described.

Jersild and Kristjansen<sup>4</sup> in 1928 reported a case of the condition, of four years' duration, in a 51 year old man, the eruption was an incidental finding, as he was being treated for tenosynovitis. The cutaneous lesions were on the left shin, the right thigh and, to a much smaller extent, on the right shin and left thigh. They consisted of groups of confluent, pinhead-sized to lentil-sized papules, yellowish brown, usually follicular and covered with a solid grayish crust, removal of which revealed shallow, round excavations. As in previous cases, the floors of the latter proved on histologic study to represent the bases of conical keratinous pegs which extended downward into the acanthotic epidermis. None was seen actually to penetrate into the corium, the authors regarded this as a minor deviation from the picture reported by Kyrle and the others. They felt that Kyrle had considered all the alternative diagnostic possibilities.

These same authors reviewed the literature up to 1928. They felt the case presented as a moulage by Galewski at Leipzig in 1921 "did not resemble Kyrle's case." One case had been presented by Planner at Vienna in 1922, but no description of it was available. A case reported by Planner and Straszberg<sup>5</sup> differed from Kyrle's case by reason of the severe inflammatory reaction and the absolute integrity of the hair follicles. The cases of Fried<sup>2</sup> and Pawloff<sup>3</sup> were mentioned as differing from Kyrle's case in their clinical aspects. A case reported by Smeloff (reference not given) was regarded as possibly acceptable. They found no reports of the disease in the French, Scandinavian or Anglo-American literature.

3 Pawloff, P. A. Zur Kasuistik der Kyrle'schen Krankheit, *Arch f Dermat u Syph* **152** 34, 1926

4 Jersild, O., and Kristjansen, A. Un cas de la maladie de Kyrle (hyperkeratosis follicularis et para-follicularis in cutem penetrans), *Ann de dermat et syph* **9** 101 (Feb) 1928

5 Planner and Straszberg. Ueber ein eigenartige Epitheliose (Epitheliose acneiformis), *Arch f Dermat u Syph* **142** 42, 1923

Kreibich<sup>6</sup> in 1931 reported a case in which Kyrle's disease appeared to coexist with keratosis follicularis. This was of special importance in the light of the frequency with which Darier's disease had been mentioned in the differential diagnosis of the former disorder. The patient was a 19 year old glass grinder who had had lesions of keratosis follicularis on his face, scalp and neck since infancy and new lesions on the trunk and arms for about a year, characterized by crateriform papules the color of the surrounding skin, with central penetrating conical horny plugs like those described by Kyrle. Both diagnoses were confirmed histologically.

De Oreo and Benedek<sup>7</sup> in 1945 presented before the Hawaii Dermatological Society a 27 year old Negro soldier, seen because of tinea cruris, in whom lesions suggestive of Kyrle's disease were an incidental finding. The eruption consisted of several flat-topped papules, 3 to 12 mm in diameter, all with central craters filled with keratinous material. On section, as in previously reported cases, the floors of these craters were seen to form the bases of conical keratotic pegs, which penetrated downward until the epidermis appeared to be stretched and greatly thinned across their pointed apices. All the lesions were widely separated from one another. One, on the left sole, was painful and interfered with walking. The palms were not involved.

Benedek alluded in the discussion to a previous case he had observed also that of a Negro soldier and both he<sup>8</sup> and de Oreo,<sup>9</sup> subsequent to this presentation, observed about a dozen additional cases each, the patients likewise being Negro soldiers. Benedek was convinced that these cases, notwithstanding their clinical dissimilarity from Kyrle's and the other cases, were nevertheless, on the basis of the histologic changes, examples of the same disease. I am inclined to believe that this is true of the case to be reported herewith.

#### REPORT OF CASE

H. B., a 32 year old white laborer, was seen in April 1945, because of multiple, occasionally painful palmar lesions of about three years' duration. They had appeared in irregular succession during this period, and the most recent one was about six months old. Six were present on the left palm and four on the right (fig. 1). Most of the lesions were situated in a crease and consisted merely of shallow circular depressions in the horny layer, about 2 mm broad and almost as deep. One, on the fifth finger of the left hand, was situated at the summit of a papule about 6 mm in diameter. One of the lesions on the left palm had three times extruded a long pointed horny plug and thereafter had bled freely.

6 Kreibich, C. Hyperkeratose (Kyrle) und Dyskeratose (Darier), *Arch f Dermat u Syph* **163** 215, 1931.

7 De Oreo, G., and Benedek, T. Hyperkeratosis Follicularis et Para-follicularis in Cutem Penetrans (Kyrle). Case Presentation, *Arch Dermat & Syph* **54** 361 (Sept.) 1946.

8 Benedek, T. Personal communication to the author.

9 De Oreo, G. Personal communication to the author.

for a short time. All were moderately painful on pressure. No significant lesions of the skin were observed elsewhere.

The Kolmer-Wassermann and Eagle reactions of the blood were negative. The blood cell count showed only an eosinophilia amounting to 8 per cent of 6,000 leukocytes per cubic millimeter.

A row of four lesions and the single papular lesion were excised from the left hand. Sections (fig 2) showed each lesion to consist of a conical keratinous plug, the base of which formed the floor of the depressions noted clinically and the point of which protruded deeply into the skin, compressing and thinning the adjoining acanthotic epidermis immediately beneath its somewhat rounded apex. There was decided parakeratosis. The corium showed a slight and nonspecific lymphocytic infiltration in the vicinity of the lesion.



Fig 1—The patient's palms, showing crater-like depressions in the horny layer of the epidermis.

The operative sites healed cleanly, and six months later there had been no recurrence and no new lesions had developed. The remaining lesions were not bothering the patient, and he did not care to have them removed.

#### COMMENT

The histologic appearance of the lesions in this case was so striking and so similar to that reported by Jersild and Kristjansen and by Benedek—and, except for the failure of actual penetration of the plugs into the corium, that reported by the other authors cited—that it seems likely that this case belongs in the same category. The clinical resemblance of this case to the cases of Kyrle and the others, however, is virtually nil except for the individual component crateriform depressions in the skin. In no reported case has the patient even had involvement of the palms, let alone limitation of distribution to that site.



Fig 2—Section of the lesion from the fifth finger, showing the characteristic conical keratotic and parakeratotic plug displacing the epidermis downward. Hematoxylin and eosin  $\times 40$ .

Kyrle's name for the disease—hyperkeratosis follicularis et para-follicularis in cutem penetrans—is an unwieldy one and seems needlessly so. From the descriptions in the literature, the lesions do not seem to occur invariably in or beside follicles, they also occur between follicles and in sweat ducts on occasion. In my own case follicles were not involved at all, and in Benedek's they were involved only occasionally. Moreover, the follicular or para-follicular location of the lesions in the other cases did not enter into the differential diagnosis. The phrase "in cutem" also seems superfluous, partly because actual penetration into the corium does not seem to be an invariable feature of the disease and partly because there is, after all, no other place for the penetration to occur if it does happen to be present. The shortened name "hyperkeratosis penetrans" appears to say all that is really necessary about the disease, and it is easier to say and to print.

#### SUMMARY AND CONCLUSIONS

A possible variant of hyperkeratosis follicularis et para-follicularis in cutem penetrans (Kyrle), limited to the palms, is reported.

"Hyperkeratosis penetrans" is suggested as an adequate contraction of the somewhat unwieldy original name of the disease.

# CONGENITAL ABSENCE OF THE VALVES IN THE VEINS AS A CAUSE OF VARICOSITIES

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AND

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THERE is little doubt that thrombophlebitis is the commonest cause of varicose veins. However, this should not make one oblivious to other factors which may also produce varices. It is becoming more evident that congenital defects of the veins or their valves are not uncommon and may explain why a young person without previous history of phlebitis or thrombophlebitis occasionally may have extensive varicose veins, with associated hemostatic dermatitis or even ulceration.

In 1936 Weber<sup>1</sup> stated

In some such cases "congenital varicose veins" [are] connected with and constitute a part of [a] developmental disturbance of growth, and [are] associated with a telangiectatic or other haemangiectatic naevus-formation.

Such "congenital varicose veins" are really only large or *giant* veins of developmental origin, but are not, strictly speaking, true varicose veins, i. e., veins with the special alteration in the vessel-walls due to insufficiency of vein-valves and chronic distension of postural origin. The large size of these "giant veins" is due to a developmental enlargement, strictly analogous to the developmental enlargement of the capillaries which is the cause of a cutaneous port-wine naevus or any variety of telangiectatic naevus.

Later Edwards,<sup>2</sup> after a study of the saphenous valves in varicose veins, concluded that most of the varices either were spontaneous in origin or followed phlebitis of the deep veins. In these two groups of varices, the valve cusps showed no profound intrinsic lesions. The fundamental lesion was a dilatation of the commissural region between the attachment of the cusps of the valves. This gave rise to an evagination of the wall and a separation of the cusps. Secondary changes of a reparative nature were seen.

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1 Weber, F. P. A Note on So-Called "Congenital Varicose Veins," Brit J Child Dis **33** 102 (April-June) 1936

2 Edwards, J. E. and Edwards, E. A. The Saphenous Valves in Varicose Veins Am Heart J **19** 338 (March) 1940

Eger and Casper<sup>3</sup> published work in 1943 supporting the theory that congenital absence of valves in the external iliac and femoral veins might be an important factor in the production of varicose veins

They showed that, as there are no valves in the superior vena cava and common iliac veins, it becomes the role of the valves in the external iliac and femoral veins to support the column of blood when one is in the upright position. Likewise, if there is a congenital absence of valves in the external iliac veins, the weight of this column of blood then must be supported by the femoral veins. If there are no valves in the external iliac or femoral veins above the orifices of the great saphenous systems, a still greater burden is placed on the valves of the latter vessels, which theoretically should be enough to lead to the eventual production of varicosities.

In 38 adult cadavers examined by them, they found that neither the external iliac nor the femoral veins contained more than one valve. In 36.8 per cent there was a total absence of valves in the external iliac and femoral veins on one or both sides. In 28.9 per cent a unilateral absence of valves occurred. In approximately 8 per cent both external iliac and both femoral veins had no valves. If these percentages are interpreted in the light of potential incidence of varicose veins occurring in the lower extremities due to the absence of valves in these veins, varicosities should develop in approximately 30 per cent of persons unilaterally and 8 per cent bilaterally.

We believe that the following report of a case supports clinically the findings of Eger and Casper in cadavers.

#### REPORT OF A CASE

A white youth aged 20 was first seen in the University Hospital May 8, 1944, with the complaint of swelling and ulcers of the right leg.

In 1937 enlargement of the veins on the right leg was first noticed. Early in 1943 his right ankle began to swell, and in August 1943 a small ulcer appeared in the region of the right medial malleolus. This was treated with sulfathiazole powder and supporting bandages, but it did not heal. Six months later new ulcers developed on the lower anterior third of the right leg, and nine months after the original ulcer appeared an ulcer occurred on the medial aspect of the right thigh.

Examination showed a tall, well developed, though poorly nourished white youth. Results of physical examination were normal except for the following findings. On the lower part of the abdomen and the legs all the veins of the larger systems were plainly seen when the patient was standing. A deep, secondarily infected ulceration was present on the medial aspect of the right ankle. Superficial ulcers were also present on the anterior and lateral sites of this ankle. Surrounding the ulcerated areas the skin was erythematous, edematous.

3 Eger, S. A., and Casper, S. L. Etiology of Varicose Veins from an Anatomic Aspect, Based on Dissection of Thirty-Eight Adult Cadavers, *J. A. M. A.* 123:148 (Sept. 18) 1943.

and weeping. A pustular, superficial, circular, slightly raised lesion about 4 cm in diameter, with some erythema, exudation and central necrosis, was present on the medial aspect of the right thigh.

The left leg had many large varices but no stasic dermatitis or ulceration. The nodes in the right inguinal region were slightly enlarged (fig 1).



Fig 1—Location of the ulcers and the residual dermatitis on the right leg. Unfortunately, the photograph was taken after surgical excision of the bed of veins in the right inguinal region.

*Laboratory Findings*—The blood pressure was 120 systolic and 80 diastolic, the pulse rate 80, the respiratory rate 18 and the hemoglobin content 77 per cent. The white blood cell count was 17,600. A roentgenogram of the chest was normal. The Kahn serologic reaction was negative. The urine was normal. The tuberculin test elicited a negative reaction to a dilution of 1:10,000 in forty-eight hours. Smears and cultures of material from the ulcer had no acid-fast bacilli in them.

Several biopsy specimens taken from the border of the ulcer showed nothing but chronic ulceration and granulation tissue. There were no changes suggestive of tuberculosis, sporotrichosis, actinomycosis or blastomycosis.

*Course in the Hospital*—On May 25, 1944, the patient was admitted to the hospital and the ulcerated areas were treated with wet dressings. One gram of sulfadiazine was given every four hours for five days with 0.65 Gm of sodium bicarbonate. His course was uneventful, and on June 8 the veins on the right side were ligated and excised. A complete absence of valves in the superficial, epigastric and upper saphenous systems was found. A remnant of a valve was present in the second section of the saphenous vein, showing incomplete development. Large varicosities and aneurysmal dilatations were present throughout the upper veins in this excised portion (fig 2).

On June 15 a 6 inch (15 cm) strip of incompetent veins in the calf and their communicating branches were excised. The small ulcers had now all healed, and the larger one was healing.

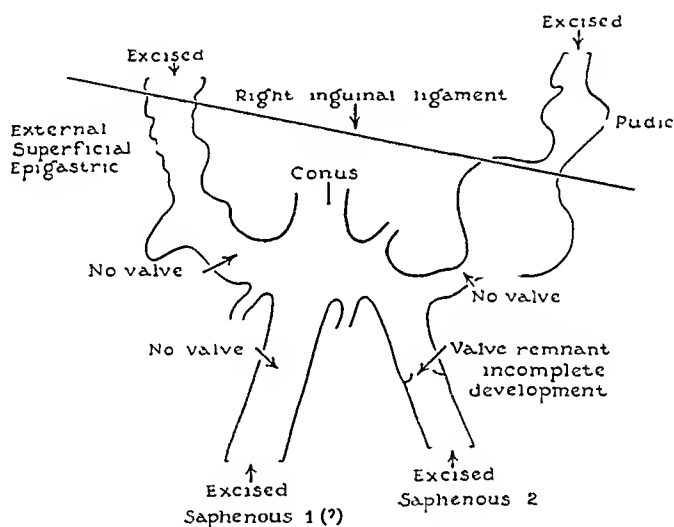


Fig 2—The excised veins from the right inguinal region. The external superficial epigastric and pudic veins had no valves. The pudic had an aneurysmal dilatation in its midportion. The conus, which represents the junction of the femoral vein to this venous bed and the first section of the saphenous vein, had no valves. The second section of the saphenous vein had a small nonfunctioning remnant in its midportion.

A ligation in the high saphenous system on the left side and excision were performed July 10, and on August 16 four ligations of small veins in the upper half of the right leg were performed. All ulcers had now healed, and evidence of hemostatic dermatitis had disappeared.

#### SUMMARY

The observations in this patient are illustrative of a congenital absence of valves in the veins of a large section of venous bed surgically removed from the right inguinal region. The veins were incised and examined after removal, and the external superficial epigastric and pudic branches had no valves. The conus, which represents the end of the

femoral vein, had no valves. The saphenous vein was double—a not uncommon finding—and no valves were present in the upper part of the first section of the saphenous vein. In the upper part of the second section a small, nonfunctioning remnant was present (fig 2). It is our belief that this case illustrates abnormal findings in the veins similar to those reported by Eger and Casper<sup>3</sup> and that these congenital abnormalities of the valves of the vein are probably only a part of a similar abnormality in other veins not removed. This abnormality could easily explain the presence of varicosities and ulcerations found in this patient. Unilateral and bilateral absence of valves in the external iliac and femoral veins of cadavers shown by Eger and Casper<sup>3</sup> should indicate that such congenital anomalies can be a cause of varicosities, hemostatic dermatitis and ulceration of the legs. Too often, preexisting thrombophlebitis is assumed to be the etiologic agent of varicose veins. In young persons who lack the history of causative factors capable of producing varicosities, the congenital absence of valves in the larger veins of the femoral and external iliac systems should be considered.

# TREATMENT OF EARLY ACQUIRED SYPHILIS WITH 600,000 UNITS OF SODIUM PENICILLIN

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SOON after the demonstration by Mahoney, Arnold and Harris<sup>1</sup> that penicillin was effective against *Treponema pallidum*, a number of investigators<sup>2</sup> reported the early effect of penicillin treatment as characterized by the disappearance of organisms from surface lesions, the healing of lesions and the reversal of serologic reactions

It is the purpose of this paper to describe the results of treatment of 34 patients on an assigned schedule of treatment of 600,000 units<sup>3</sup>. A follow-up of 100 per cent of the cases for at least a year has afforded an unusual opportunity to observe the results of the time-dosage schedule employed

Miss Josephine Long and Miss Alice Carter furnished technical assistance

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This investigation was made under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the University of Virginia. E. R. Squibb & Sons contributed to the support of this study

1 Mahoney, J. F., Arnold, R. C., and Harris, A. Penicillin Treatment of Early Syphilis, *Am J Pub Health* **33** 1387 (Dec.) 1943

2 Bloomfield, A. L., Rantz, L. A., and Kirby, W. M. M. The Clinical Use of Penicillin, *J A M A* **124** 627 (March 4) 1944. Wise, C. R., and Pillsbury, D. M. Penicillin in the Treatment of Syphilis, *Proc Roy Soc Med* **37** 491 (July) 1944. Mahoney, J. F., Arnold, R. C., Sterner, B. L., Harris, A., and Zwally, M. R. Penicillin Treatment of Early Syphilis, *J A M A* **126** 63 (Sept. 9) 1944. Ross, A. O. F., Nelson, R. B., Lowrie, E. M., and Collier, H. O. J. Treatment of Early Syphilis with Penicillin, *Lancet* **2** 845 (Dec. 30) 1944. Binkley, G. W., and Kile, R. L. Rapid Treatment of Early Syphilis with Small Doses of Penicillin, *Arch Dermat & Syph* **51** 200 (March) 1945

3 Moore, J. E., Mahoney, J. F., Schwartz, W., Sternberg, T., and Wood, W. B. The Treatment of Early Syphilis with Penicillin, *J A M A* **126** 67 (Sept. 9) 1944

## METHOD OF STUDY

Between April 1, 1944 and Nov 1, 1944, there were 34 patients with early acquired syphilis treated with penicillin on a schedule of 600,000 units given over a period of four days. There were 13 men and 21 women, 4 of whom were white and 30 Negro patients. Their ages ranged from 14 to 42 years. Twenty-five, or 73.5 per cent, of the patients were under 25 years. All the 34 patients have been followed for a year or more. Twenty-nine have been followed for eighteen months or more, 20 for twenty-one months or more and 14 for two years or more.

In each case the diagnosis was established by the demonstration of *T pallidum* in the existing mucous or cutaneous lesions of primary or secondary syphilis. In addition, all but 2 patients with seronegative primary syphilis had positive Kahn reactions of the blood. The duration of lesions was from four to one hundred and eighty days. Twenty-five, or 73.5 per cent, of the patients had lesions of less than thirty days' duration.

When the diagnosis was established the disease in 2 patients was in the seronegative primary stage, in 8 it was in the seropositive primary stage and in 24 it was in the secondary stage. In addition to early syphilis, 7 patients had acute gonococcic urethritis.

All patients were hospitalized for four and one-half days, during which time they were given 20,000 units of sodium penicillin in 2 cc of isotonic solution of sodium chloride every three hours, day and night, for thirty intramuscular doses, a total of 600,000 units. Eight different lots of penicillin, supplied by five different manufacturers, were employed.

A Wassermann test and a titred Kahn test of the blood were performed immediately before and after treatment and twice monthly whenever possible during the period of post-treatment observation. The titred Kahn test was employed for treatment control. The cerebrospinal fluid was examined before treatment in every case and reexamined in all but 1 case six months or more after treatment. In a large number of patients determinations of icterus indexes and blood urea content were made before and after treatment. Dark field examinations of surface lesions were done every three hours or oftener in 8 cases following the first injection of penicillin. No pregnant patients were treated with this dosage.

## REACTIONS

A Herxheimer reaction was observed in 13 (38.2 per cent) patients during the first twenty-four hours of treatment. In 10 patients it was manifested by fever, chilliness, occasional headache and malaise of mild degree. In these patients the rectal temperature rose to between 99.6 and 103 F. In 2 cases the cutaneous eruption was accentuated, with increase in intensity of the eruption and edema of the mucous lesions. One patient experienced a combined febrile and cutaneous reaction. No untoward reactions to treatment, such as abdominal pain, nausea, vomiting or toxic cutaneous eruptions, were noted.

No significant abnormalities were noted in the laboratory examinations of the peripheral blood, the urine, the blood urea and the icterus index.

No interruption of treatment was necessary because of unfavorable reactions to treatment.

## RESULTS

Spirochetes in the surface lesions disappeared rapidly in all cases after institution of therapy. In 8 patients on whom dark field examinations were made every three hours or oftener, spirochetes could not be demonstrated in the lesions after a period of from eight to twenty-two and a half hours. In 2 of the 8 cases, organisms disappeared from the surface lesions in less than fifteen hours. Mucous and cutaneous lesions healed rapidly under treatment. Chancres, mucous patches and cutaneous lesions were healing well at the time of the patients' discharge from the hospital. In all but 1 case, complete healing was observed in from ten to fifty-six days.

In 2 cases of seronegative primary syphilis the chancres healed in twelve and twenty-one days respectively. In 8 cases of seropositive primary syphilis the chancres healed in from thirteen to forty-seven days, and in 23 of the 24 cases of early secondary syphilis the mucous and cutaneous lesions healed in from ten to fifty-six days. In 1 case, the secondary lesions were still present, although healing slowly, ninety-seven days following treatment. At this time, relapse occurred and spirochetes were demonstrated in surface lesions.

At the time of the last observation 20 patients were seronegative and free of symptoms. These patients have been followed for from four hundred and nineteen to seven hundred and eighty-five days. Only 4 cases have been followed for less than eighteen months. Of the total patients, 2 had seronegative primary syphilis. Of the seropositive patients, seroreversal occurred up to two hundred and twenty-eight days after treatment. Eight patients became seronegative in less than ninety days after treatment. Eleven patients relapsed in from ninety-seven to three hundred and seventy-six days. Three patients still had some reagin in the blood at the time of the last examination.

Seven patients who also had concomitant gonococcic urethritis obtained a favorable therapeutic result, with complete disappearance of this infection by the time of discharge from the hospital.

## RELAPSES

Data on the cases in which relapse occurred following treatment are given in the accompanying table. There were 11 instances of relapse, in all of which the patients were retreated on heavier doses of penicillin. Ten relapses occurred in patients with secondary syphilis and one in a patient with seropositive primary syphilis. Three patients with secondary syphilis were classified as having serologic relapse on the basis of sustained increase in titer on two consecutive examinations. In the remaining 8 patients there developed mucous and cutaneous lesions from which spirochetes were recovered, with an accompanying serologic relapse.

Among the patients with secondary syphilis who relapsed was one who had minimal abnormality of the cerebrospinal fluid, characterized by fourteen cells. There were no cases of neurologic relapse. In none of the 11 cases of relapse could reinfections be demonstrated. Relapses occurred at from ninety-seven to three hundred and seventy-six days with an average of two hundred and nine days.

#### EXAMINATION OF THE CEREBROSPINAL FLUID

Only 2 of the 34 patients showed any abnormality in the cerebrospinal fluid, in both of whom it was characterized by an increase in cell count. One patient with seronegative primary syphilis had 13 cells per cubic millimeter. The other, a patient with secondary syphilis, showed

#### *Relapses on Treatment with 600,000 Units of Penicillin, Classified According to Stage of Disease, Type of Relapse and Time of Appearance*

Case No	Stage of Disease	Type of Relapse	No. of Days after Treatment That Relapse Was Discovered
2	Secondary	Serologic	259
3	Secondary	Mucocutaneous	234
8	Secondary	Mucocutaneous	281
16	Secondary	Mucocutaneous	347
19	Seropositive primary	Mucocutaneous	124
23	Secondary	Mucocutaneous	200
26	Secondary	Mucocutaneous	110
28	Secondary	Serologic	135
33	Secondary	Mucocutaneous	97
34	Secondary	Mucocutaneous	145
38	Secondary	Serologic	376

14 cells per cubic millimeter. This patient was found to have a mucocutaneous relapse with normal cerebrospinal fluid when reexamined one hundred and twenty days after treatment.

#### COMMENT

It has been adequately demonstrated with both penicillin therapy<sup>3</sup> and intensive arsenical therapy<sup>4</sup> that, regardless of the ultimate dosage, there is immediate disappearance of spirochetes from the surface lesions, healing of lesions and tendency toward reversal of serologic reactions. This effect is obtained even with the inadequate dosage of 60,000 to 300,000 units of penicillin.<sup>3</sup> The effectiveness of a treatment schedule must thus be judged by the incidence of clinical and serologic relapse, which can only be detected on prolonged observation. Only 5 of the 11 cases of relapse occurred during the first six months after completion of treatment. While opportunity for reinfection was present in none of the 11 cases could the criteria for reinfection be met.

<sup>4</sup> Leifer, W., Chargin, L., and Hyman, H. T. Massive Dose Arsenotherapy by Intravenous Drip Method. *J. A. M. A.* **117**: 1154 (Oct. 4) 1941.

In the present series of 34 patients there was an incidence of observed relapse of 32.3 per cent. Two patients with seronegative primary syphilis were well at five hundred and forty-eight and seven hundred and sixty days. Seven of the 8 patients with seropositive primary syphilis were well at from four hundred and nineteen to seven hundred and fifteen days, with only one relapse. The greatest incidence of relapse was encountered in the group of patients with secondary syphilis, in which 10, or 41.6 per cent, of the patients relapsed. Of the patients with relapsed secondary syphilis there were 7 (29.1 per cent) who had mucocutaneous relapses, at from ninety-six to three hundred and forty-seven days, and 3 (12.5 per cent) serologic relapses, at from one hundred and thirty-five to three hundred and seventy-six days.

There was a disquieting incidence of late relapse. Although in 5 it occurred within less than six months following treatment, in the remaining 6 it appeared after six months. There was 1 case of serologic relapse as late as three hundred and seventy-six days.

Three patients still under observation are showing some degree of seroresistance manifested by persistent reagin in the blood at from three hundred and eighty-three to six hundred and twenty-seven days. The therapeutic issue must remain doubtful in these patients. In view of the high incidence of relapse in this series, seroresistance can be regarded only as an unfavorable response to treatment. There are thus only 20 patients, or 58.8 per cent of the total, whose serum gave a negative reaction and who were asymptomatic, and who may be regarded as having obtained a favorable result from treatment.

Interpretation of these results must be made with due regard for the changing character of commercial penicillin<sup>5</sup>. It is believed that the patients described in this paper were treated at a time when the therapeutic efficacy of penicillin was superior to that available at present (June 1946).

#### SUMMARY AND CONCLUSIONS

Thirty-four patients with early syphilis were treated with 600,000 units of penicillin given intramuscularly over a period of four days. All cases were followed for a year or more. Twenty-nine were followed for eighteen months or more, 20 for twenty-one months or more and 14 for two years or more.

An immediate, favorable treatment response, characterized by disappearance of spirochetes from surface lesions, healing of lesions and prompt decrease in serologic titer, was noted.

5 The Changing Character of Commercial Penicillin, the Committee on Medical Research, the United States Health Service and the Food and Drug Administration, *J A M A* 131:271 (May 25) 1946.

There were 11 (32.3 per cent) cases of mucocutaneous or serologic relapse. The greatest incidence of relapse was observed in cases of secondary syphilis. The serum of 3 patients is still resistant.

Only 20 patients, or 58.8 per cent of the total, were both seronegative and asymptomatic at the end of the period of observation. These patients may be regarded as having obtained a favorable result from treatment.

In view of the already high incidence of relapse and with the possibility of further relapse, it can be concluded that penicillin in a dosage of 600,000 units is inadequate for the treatment of early syphilis.

## RELAPSING SYPHILIDS OF THE GENITALIA

Persistence of Lesions Seven Months After Serologic Reversion

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HABANA, CUBA

**B**ECAUSE of special involution of the lesions in a case of relapsing syphilids of the genitalia, a similar type of which I have not previously observed (nor have I been able to find any reference thereto in the literature), I am presenting a resume of my observation, in the hope that I may be enlightened in finding a possible interpretation of the paradoxical facts that I have observed

### REPORT OF A CASE

R G, a white law student aged 25 years, weighing 160 pounds (72.6 Kg), gave the history of a penile sore of the frenum early in July 1944. The lesion was examined and treated as soft chancre. On August 28, the serologic reaction was strongly positive. Weekly or every ten days, injections of neoarsphenamine, 0.60 Gm, were given during September and October, the patient was then dismissed without serologic control or further instructions.

On Jan 5, 1945, he asked my advice regarding lesions that had developed seven weeks previously. These were limited to the glans penis and its foreskin, the rest of the mucous membranes and skin being free. Generalized enlargement of the lymph nodes was observed. Spirochetes were demonstrated in the lymph from the inguinal nodes. The lesion that occupied most of the glans penis exhibited polycyclic borders and a rough clover leaf contour. Raised and deeply infiltrated, the entire thickness of the skin was involved, being therefore firm and solid to the touch. The color was a dull brownish red, and the surface was intact, dry and nonscaly. Two similar lesions, the size of a large pea and round, were located in the foreskin. The diagnosis of mucocutaneous relapse was established, the lesions presenting characteristics which in some respects differed from those of common secondary syphilids. Inadequate treatment induced in an early stage the development of lesions presenting some of the features of tertiary manifestations. The Wassermann and Kahn reactions were strongly positive. On examination the spinal fluid proved normal. The patient received twenty-five injections of oxophenarsine hydrochloride, 0.06 Gm, one every three days, and one weekly injection of bismuth subsalicylate for a total of ten. On March 31 the Wassermann and Kahn reactions were strongly positive and the lesions remained unchanged, no new elements having appeared.

Read at the Sixty-Sixth Annual Meeting of the American Dermatological Association, Hot Springs, Va., June 11, 1946

From the Department of Dermatology and Syphilology of the University of Havana Medical School and the Mercedes Hospital, Braulio Saenz, M D, Director



FIG 1—*A*, slight acanthosis and hyperkeratosis. Atrophy of the corium is less pronounced in the vicinity of the papillae. There is a diffuse infiltrate, mostly consisting of plasma cells. *B*, pronounced panvasculitis, although total obliteration is not observed.

A positive serologic reaction after such treatment is a commonly observed fact, but not so the lack of action on the lesions, which did not show any tendency to regression. The clinical diagnosis, established on the bases of history, clinical symptoms, results of dark field examination and serologic findings, required at this moment histopathologic confirmation.

Histopathologic examination showed slight acanthosis and hyperkeratosis and atrophy of the corium, less pronounced in the vicinity of the papillae. Here existed a diffuse infiltrate, mostly consisting of plasma cells (fig 1 *A*).

Pronounced hyperplasia of the collagenous fibers of the corium was present, with abundant newly formed blood vessels. These presented definite panvasculitis, although total obliteration was not observed (fig 1 *B*). There were areas



Fig 2—Areas of infiltration around the blood vessels, consisting of round cells, numerous plasma cells, epithelioid cells and a few giant cells

of infiltration, more pronounced around the blood vessels, consisting of round cells, numerous plasma cells, epithelioid cells and few giant cells (fig 2). This picture corresponded to secondary syphilids.

The failure of the energetic arsenical therapy supplemented with bismuth subsalicylate to cause involution of the lesions indicated that the patient, otherwise healthy and in perfect hygienic condition, was arsenic-bismuth resistant. In an effort to control resistance to treatment, the patient having refused the use of arsphenamine because the neoarsphenamine had been badly tolerated, it was determined to use penicillin instead of nonspecific measures.

A total of 4,800,000 Oxford units was administered in intragluteal injections during fifteen days, ending April 20, conjointly with 6 Gm a day of iodide of potassium by mouth for one month. After ten days of penicillin, the Wassermann and Kahn reactions were moderately positive, and they were totally reversed two

weeks later, on May 15. At that time the lesions had not been influenced by the therapy. The usually observed correlation between the behavior of the serologic reactions and the clinical symptoms was lacking.

From May 20 to July 20 and from August 25 to October 25, the patient received two courses of twenty injections of oxophenarsine hydrochloride, 0.06 Gm, and fifteen injections of bismuth subsalicylate. In between these two courses, 4,800,000 Oxford units of penicillin was given in fifteen days, preceded and followed by 6 Gm per day of iodide of potassium.

At that time the involution of the lesions had started in the central parts, and one month later, on November 20, the two lesions of the foreskin had undergone reabsorption, the one on the glans penis presenting the aspect of four lentil-sized papules, slightly raised and dry (fig 3).



Fig 3—Aspect of the lesions on November 20, four lentil-sized papules on the glans penis remaining of the original lesions. The two lesions of the foreskin had undergone reabsorption.

The total regression was completed in about four weeks, seven months after the serologic reaction had been reversed. The surface appeared thinned and wrinkled, as observed in superficial atrophy. Serologic reactions and spinal fluid have remained normal ever since April 20. The cardiovascular system was normal.

#### COMMENT

The extremely slow involution of the lesions in this case did not coincide with the serologic reversion, as is commonly observed, this was achieved after combined arsenical-bismuth therapy was complemented with penicillin and iodide of potassium. Two more arsenic-bismuth courses and between these, one more treatment with penicillin and iodide of potassium were necessary to determine the total involution of the lesions seven months after the serologic reversal had occurred.

The hypothesis of an existing anergy is in this case untenable and also contradicted by the reversion of the serologic reaction and the non-appearance of new lesions. The explanation may be dependent on the

profound changes of the blood vessels and subsequent coherence of the infiltration. Nevertheless, the histopathologic picture is no different from that observed in common relapses of this type.

Being unable to offer a satisfactory answer to the aforementioned facts, I am presenting the case in an effort to obtain a correct interpretation.

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#### ABSTRACT OF DISCUSSION

DR SAMUEL E. SWEITZER, Minneapolis. The diminishing response that some think is being derived from penicillin might be due, as is stated, to an increasing resistance of the organism. In the laboratory, in order to get an increase in resistance to a drug, small doses must be given over a long period to build up resistance to that drug in the certain disease organism. How, in the few years' time that penicillin has been used—just a short time—can one expect a spirochete to develop resistance to penicillin? For penicillin cures, say, 80 per cent, with perhaps 16 to 20 per cent of failures, so there would be 80 per cent of the patients that would be cured in the first place and they could not give the disease to anybody, and that would leave only 20 per cent to infect others. So I myself think that that one can be crossed off.

The other question is, what has happened to the penicillin? Also, nothing has been stated as to how penicillin is made. It is an organism that is grown on mediums. The mediums on which an organism is grown give varying types and strengths of the organism that is being grown. One can tell that by ringworm cultures. Professor Bieter, at the University of Minnesota School of Pharmacy, talked this over at staff meetings at the Minneapolis General Hospital, and he gave as an explanation of some of the diminishing value of penicillin the fact that penicillin is grown on mediums made from corn. Corn this last year was not very good, it was not so good as it had been the previous year. The corn was green, and he made the statement that the mediums on which the penicillin was grown might have an influence on the organism that is being grown and influence the value of the results that are obtained.

DR UDO J. WILE, Ann Arbor, Mich. I do not believe that the explanation offered by Dr Sweitzer is the whole story. It may well be that penicillin is not so active therapeutically today as it was a year ago. However, I do not believe that this is the sole explanation. My associates and I have been using the material for a longer time, our cases have been followed longer and I think that we are getting what I should regard as an anticipated rate of failure.

The K penicillin, which is under indictment as a possible cause for failure, has in fact been used only a short time and for a few patients.

It is entirely a Utopian point of view to expect a 100 per cent satisfactory result in any disease like syphilis, in which there will be two inevitably variable factors. The first factor is the individual patient, whose response to the infection can never be said to be uniform. The organism, likewise, is a variable factor and is subject to the same law of life with regard to the survival of the fittest as every other living thing is. For this reason, I think that it is proper to assume that there may be in existence or produced resistant strains to penicillin.

I see no reason for a gloomy view of the therapy of penicillin in syphilis if 60 per cent of the patients can be cured at this time with dosages which are still unsettled and with uncertain intervals of time. This would seem to me to be a real

achievement not possible with older methods of treatment, except in rare conditions, which extended over months and years

With regard to the dosage and interval of time, it seems not unlikely that the experience of dermatologists with syphilis will parallel that of the internists in viridans endocarditis. There is some similarity between these two infections. Both are sepses characterized by intermittent recurrences with dissemination into remote parts of the body, causing focal lesions, both have a tendency to remain quiescent for months and then to relapse. The internists have found that with empiric doses of penicillin a certain percentage of their patients recovered, then after weeks and months a few relapsed. These patients received larger doses, some of those for the second time achieved cure, and still others relapsed the third time. At the present time the internists find it necessary, to get a maximum result of treatment, to give from 60,000,000 to 80,000,000 units over a period of six weeks. Even with this large dosage and long interval of time there are certain strains of viridans streptococci which are entirely resistant and with which failure occurs. If penicillin is erroneously dosed today in the treatment of syphilis, I am convinced that patients are being underdosed rather than overdosed. Ultimately, much larger doses may have to be given, but they will sound less astronomic when they are specified in terms of milligrams instead of in terms of units.

DR NORMAN H EPSTEIN, San Francisco. I think that the case presented by Dr Saenz is interesting and certainly unusual. This case must be accepted as one of relapsing syphilis, with the patient resistant to arsenical drugs and also penicillin.

Dr Saenz had an opportunity to make use of nonspecific measures locally in his case. It is known that *T pallidum* does not resist temperatures of 41 C for more than an hour. Local heat might have been used in the treatment of the lesion. The use of nonspecific measures generally, such as artificial fever therapy of course, is recognized as being of value in this type of case. I think perhaps that it might have altered the course of the disease.

The papers on penicillin therapy which were presented here two years ago naturally stimulated the enthusiasm of every one in the use of penicillin in the treatment of syphilis. When penicillin became available, efforts were concentrated on the treatment of neurosyphilis, combining penicillin and fever therapy. Forty thousand units of sodium penicillin intramuscularly were given every three hours for fourteen days. This treatment was combined with artificial fever. The artificial fever was given usually on the third, seventh and tenth day and, if possible, on the fourteenth day. Fever was continued weekly until the patient had received fifty hours of fever.

I have only impressions as to the therapeutic effects of this regimen. The most striking effect of penicillin therapy combined with fever was on the spinal fluid. It was particularly notable in the group III types of fluid. My colleagues and I had one example of a young person with dementia paralytica who was confused and disoriented and had to be sent to a state institution, where he was given malarial therapy. He improved clinically sufficiently to return to work and then was referred back for further treatment. Sixteen months later, the spinal fluid was a group III fluid, four months after penicillin and fever therapy, the spinal fluid was essentially normal.

That is not an isolated instance, as there were many of that character, but, on the other hand, there were certainly a number of patients in whom the effect on the spinal fluid was disappointing. There were a number of others in which the colloidal gold curve flattened out so promptly that I think it can be said that it was not the fever therapy alone but that penicillin contributed to this result. We have

seen a better response to a combination of penicillin and fever therapy than to either alone

DR V PARDO-CASTELLO, Habana, Cuba I really have no definite explanation to offer as to the cause of the resistance to treatment of Dr Saenz' patient I have been thinking ever since he told me about his case of several possible explanations One of them is local infection I remember in the old days when local syphilitic lesions would not heal readily they were treated with the old mercury plasters I do not think that the mercurial plasters in such cases acted in any specific way but as an aid in removing the secondary infection that will not allow healing under any specific treatment However, most secondary organisms in this case would have yielded to the treatment with penicillin

I think that the most scientific explanation one could offer would be a lack of response on the part of the patient I think that it is a case in which although syphilis is being treated the syphilitic patient is not being treated, and that perhaps fever therapy or nonspecific treatment such as the injection of liver extract or injection of milk protein would have helped

In some of these cases, exposure to ultraviolet light has been tried, with a certain measure of success, producing, of course, a certain amount of cutaneous reaction

That would be the explanation that I should offer as being to my own satisfaction for the case of Dr Saenz

If I may be permitted to say something about penicillin, I should say that I was interested from the beginning, because the Cuban government made me the comptroller of penicillin for Cuba, and I was glad to hear of the comparison Dr Wile made between syphilis and chronic endocarditis I had, in the beginning, refused the use of penicillin for endocarditis, because that is what my associates and I were told to do, until the physicians convinced me that the patients were improving, then we had to grant a certain amount of penicillin for these patients, and a number of them did get well

I firmly believe that the same thing will be done with penicillin as was done with the arsphenamines In the year 1912, when I was a student intern in my hospital, the arsenicals began to be used First one injection would cure the patient, then it would be three or four, and then it would be a course of six or eight, until finally it was decided that there had to be repeated courses of arsphenamine I think that we are going to have repeated courses of several million units of penicillin at intervals, maybe, and I hope that that will be the answer, together with the arsenicals and the bismuth preparations as they are used today I think that it will have to be done in some way that will not necessitate giving injections to the patient every three hours

I have been much disappointed, too, with the results of penicillin in late syphilis, particularly in syphilis of the nervous system

DR DUDLEY C SMITH, Charlottesville, Va This is an endless subject I should like to say a few more words about the trend in the use of penicillin The work that I reported here was a schedule that was started under the supervision of the National Research Council There has been a tendency to increase the dosage After this schedule was used in our clinic, we increased the dose to 2,400,000 Recently the schedule has been changed, and we are using 9,600,000 units over a period of fifteen days (80,000 units intramuscularly every three hours day and night)

The final answer has not been worked out We do not know what the best schedule is, but we do know that small dosages do not give uniformly good results Additional experience may indicate the desirability of, first, giving more penicillin at each injection, second, shortening the interval between injections, third,

lengthening the total time and dosage, fourth, repeating courses of treatment, or, fifth, employing other supplemental therapeutic agents

Some explanation of the increase of the proportion of penicillin K in commercial penicillin should be recorded. When the manufacturers were urged to increase their output of penicillin, they inaugurated several changes. Adjuvants were added to the mediums to stimulate the growth of the mold and also to cause the production of penicillin throughout the contents of the vats in which the mold was growing. In addition to adjuvants and other laboratory cultural changes, the strain of penicillin was changed. The manufacturers were being urged by governmental authorities and all others concerned to produce more penicillin, which they did. This penicillin tested out in the laboratory satisfactorily and seemed to meet all the required standards. On the Petri plate and in the test tube, it passed the tests that were required by the Food and Drug Administration. It was later discovered, though, that the results in the treatment of syphilis, as well as other infections, were not so good as those obtained with penicillin previously. The explanation of the lower therapeutic index of this penicillin was thought to be an increase of penicillin K.

After penicillin had been separated into its several fractions—F, G, X and K—it was discovered that penicillin K did not give a sustained blood level for more than about twenty minutes. In addition, it could not be recovered from the urine in amounts corresponding to that administered. This was interpreted to mean that penicillin K was destroyed or neutralized in the tissues, and this was thought to be the basis for the poor clinical results. The rapidly produced penicillin contained as much as 80 to 90 per cent of K, as compared with 10 to 20 per cent in the original commercial penicillin. I understand that this is now being corrected and that the penicillin being made at the present time, or certainly in the near future, will contain about 80 to 90 per cent penicillin G, with less K.

Freedom of persons to try out different schemes of management, as suggested by Dr O'Leary, is desirable, however, it is necessary to pool the therapeutic results obtained with varying dosage in early syphilis in order that minimum standards of cure can be more quickly obtained. As I said earlier, a small group of cases will prove the inadequacy of a poor time-dosage schedule, but when the scheme of treatment approaches a curative standard a larger group of cases and more time are necessary for reaching a definite conclusion.

# LEISHMANIA VACCINE TEST IN LEISHMANIASIS OF THE SKIN (ORIENTAL SORE)

## Quantitative Experiments

F SAGHER, M D

JERUSALEM, PALESTINE

**T**HE POSITIVE result of an intracutaneous leishmania vaccine test indicates that a person is going or has gone through an infection of leishmaniasis cutis. No information can, however, be derived from the outcome of the test as to the special type of leishmaniasis, which in this part of the world shows great diversity in its aspect and development.

When tests are performed on a large material it has been noted that the same dose that in one infected person provokes a necrotic reaction is in another scarcely able to elicit a positive response at all. It was, therefore, interesting to study the law underlying this peculiar phenomenon.

While in connection with tuberculosis this question offers great difficulty, since a large proportion of all adults give a positive reaction anyway, my associates and I were in the case of leishmaniasis guided by the more or less characteristic scar which is invariably left behind by the primary lesion of the skin. Jadassohn,<sup>1</sup> Martenstein and Noll,<sup>2</sup> Scholtz,<sup>3</sup> Sulzberger and Wise,<sup>4</sup> Bonnevie and With,<sup>5</sup> Bonnevie and Bjørnstad<sup>6</sup> and others were able to show that certain tuberculous condi-

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1 Jadassohn, J. Remarks on Tuberculin in Dermatology, *Brit J Dermat* **41** 451-472 (Dec) 1929

2 Martenstein, H., and Noll, R. Statistische Untersuchungen über die Tuberkulinreaktion, *Arch f Dermat u Syph* **158** 409, 1929

3 Scholtz, W. Ueber Wert und Spezifität der Tuberkulinreaktion bei Luposen, *Dermat Ztschr* **53** 775-777 (April) 1928

4 Sulzberger, M B., and Wise, F. Tuberculin. Newer Dermatological Considerations and Reasons for Its More General Use in Diagnosis, *M Clin North America* **14** 1555-1568 (May) 1931

5 Bonnevie, P., and With, T K. Quantitative Untersuchungen zur Tuberkulinreaktion (mit der gradierten Intracutanmethodik) bei verschiedenen Formen von Hauttuberkulose und Tuberkuliden bzw bei tuberkulose-verdächtigen Hautkrankheiten, *Arch f Dermat u Syph* **175** 181-205, 1937, cited by Bonnevie and Bjørnstad<sup>6</sup>

6 Bonnevie, P., and Bjørnstad, R. Clinical Tuberculin Diagnostic by Means of Weak Intracutaneous Doses, with Special Regard to Tuberculous Skin Diseases, *Acta dermat-venereol* **21** 9-37 (Feb) 1940

tions of the skin were characterized by a difference in their reaction to lower concentrations of tuberculin, and it seemed probable that in cutaneous leishmaniasis too the different manifestations would be characterized by a different reaction to graded concentrations of vaccine

*Experimental Setup* The studies described in the following paragraphs were carried out in the years 1941 to 1943. As to details of the vaccine used, the reader is referred to Dostrovsky.<sup>7</sup> The vaccine was freshly prepared every three months in winter and every four to six weeks in summer. The original concentration was of 1,000,000 leishmania parasites per cubic centimeter. This original solution was used in the following dilutions, which were bottled in special flasks so that the same flask could be used for a number of experiments

No. of parasites per 0.1 cc	Original Solution	1:10	1:100	1:1,000	1:10,000	1:100,000	1:1,000,000	1:10,000,000
	100,000	10,000	1,000	100	10	1	0	0

Injectons were started with the lowest concentration, proceeding to the next higher concentration, in order to avoid the remaining in the syringe of remnants of a higher concentration. The injections were, without exception, given intracutaneously at the inner aspect of the arm and forearm.

As it was not always possible to give the entire series of injections on one occasion, it was tried to get a general idea of the degree of sensitivity by a high, a medium strong and a low concentration, the accurate grading following in a second sitting. At the same time control tests were set up with tuberculin in concentrations of 1:100,000 or 1:50,000 or a 0.5 per cent phenol solution. The reactions were watched for from forty-eight hours to one week and only in exceptional cases for longer periods.

Reactions having, after forty-eight hours, developed to a diameter of 0.5 cm. were marked 1 plus, those from 1.0 to 1.5 cm. were marked 2 plus and those more than 1.5 cm. were marked 3 plus. Reactions smaller than 0.5 cm. were neglected, since their distinction from traumatic reactions is too difficult and results may, therefore, become confused.

Tests were set up in a total of 84 cases of leishmaniasis cutis and in 74 controls presenting various kinds of dermatoses. Of these controls, 72 yielded a negative reaction, while 2 gave a positive reaction. Both patients with positive reactions had extensive furunculosis.

Among the 84 patients with leishmaniasis, 50 were once, 20 twice and 14 three times submitted to a full series of tests in which partly the same and partly freshly prepared vaccine was used, in some cases after an interval of up to two years.

<sup>7</sup> Dostrovsky, A. The Diagnostic Value of Leishmania Vaccine, *Ann. Trop. Med.* 29:123-128 (July) 1935.

The cases were grouped as follows

1 *Leishmaniasis Nodosa (Early Stage)*—The term leishmaniasis nodosa was applied in all cases in which the process had been present for up to one year, including the ulcerative types. Histologically, these forms are, as a rule, characterized by the presence of chronic, nonspecific inflammation.

2 *Leishmaniasis Recidiva (Late Stage)*—Leishmaniasis recidiva includes any process present for more than one year. Clinically, it is characterized by its resemblance to the lupoid forms of tuberculosis or

TABLE 1—*The Upper Limit of Sensitivity Toward Graded Concentrations of Parasites in Leishmania-Vaccine in the Different Types and Stages of Cutaneous Leishmaniasis*

	Anergic Reactions Negative		Hyperergic		Normergic		Hyperergic			No of Patients
	Original	Original	1 10	1 100	Dilution		1 100,000	1 1,000,000	1 10,000,000	
					1 1,000	1 10,000				
					Parasites in 0.1 Cc					
					100	10				
100,000	100,000	10,000	1,000	100	10	1	0	0		
Leishmaniasis nodosa		0	1	9	5	19	3	1	0	38
Leishmaniasis recidiva	1	1	2	1	0	4	3	6	2	20
Transition forms		0	0	0	0	0	2	2	0	4
Total	1	1	3	10	5	23	8	9	2	62

gummas, while histologically the tissue is usually that of a tuberculoid granulation.

3 *Transition Forms*—Transition forms are those in which lymphogenic spread is already noted in the first year as well as annular types, i. e., manifestations indicative of a merging into the late stage.

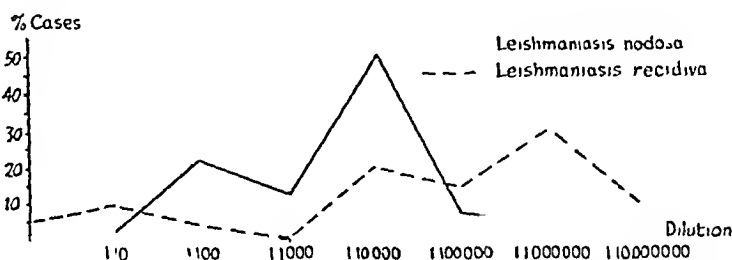
A further subdivision into too many groups according to clinical characteristics seems inadvisable. Among the 84 patients with a positive outcome of the test 22 could not be followed, and only 62 could, therefore, be accurately checked and evaluated.

From table 1 it appears that of 38 cases of leishmaniasis nodosa the reaction was positive in 34 up to a dilution of 1 10,000, the maximum lying between 1 100 and 1 10,000. No more than 4 patients had a higher sensitivity (between 1 100,000 and 1 1,000,000).

Entirely different were the results in leishmaniasis recidiva. With it out of 20 patients 15 elicited positive reactions between dilutions of 1 10,000 and 1 10,000,000. Of the other 5, 1 patient gave a nega-

tive reaction and 1 yielded a positive reaction only with the original concentration

In 7 cases of the nodular type we had the opportunity of testing the patients during the presence and after healing of the lesions, but no longer than a few weeks or months later. In 2 of these cases a distinct increase in sensitivity was noted, while in the others there was no difference at all. The transition forms also displayed a high degree of sensitivity.



A graphic representation of the distributions shown in table 1

There was further the question as to whether the number and intensity of lesions has any bearing on the intensity of the intracutaneous reaction. This is shown in table 2. From table 2 it appears that in 42 persons presenting leishmaniasis nodosa no difference as to the degree of sensitivity was noted independent of whether there were one or fifty lesions.

TABLE 2—The *Leishmania* Test in Forty-Two Cases of *Leishmaniasis Nodosa* Arranged by the Number of Lesions

No of Lesions	Orig inal	Dilution							Total Lesions
		1 10	1 100	1	1	1	1	1	
				1 000	10,000	100,000	1,000,000	10,000,000	
Parasites in 0.1 Cc									
	100,000	10,000	1,000	100	10	1	0	0	
1	0	1	5	3	5	1	0	0	15
2	0	0	1	1	3	0	0	0	5
3	0	0	2	0	1	0	0	0	3
Up to 5	0	0	0	2	4	0	0	0	6
Up to 10	0	0	1	1	4	1	0	0	7
Up to 20	0	0	1	0	2	0	0	0	3
Up to 50	0	0	0	0	2	1	0	0	3
Total	0	1	10	7	21	3	0	0	42

The sensitivity to the vaccine does not, therefore, show any parallelism to the number and severity of the lesions.

In our tabulation the immediate reactions were entirely neglected. Berberian<sup>8</sup> described a sort of positive reaction which he was able to

8 Berberian, D. A. Cutaneous Leishmaniasis (Oriental Sore). I. Time Required for Development of Immunity After Vaccination, Arch. Dermat. & Syph. 49: 433-435 (June) 1944.

produce with living leishmania cultures. In patients in whom microscopic observations were normal there developed, immediately after administration of the parasites, an immediate reaction characterized by urticaria and edema. A similar reaction is occasionally noted after application of leishmania vaccine, but we have not the impression that we are dealing with a specific response.

Apart from control tests with phenol, in 51 cases tuberculin tests were set up in dilutions of 1:50,000 and 1:100,000. Of 20 patients with recurrent leishmaniasis 15 elicited negative reactions and 5 positive reactions. Of 31 patients with leishmaniasis nodosa 22 elicited negative reactions and 9 positive reactions. These figures are to a high degree in conformity with findings concerning the sensitivity toward tuberculin in this country. In any event, the types of leishmaniasis in which the histologic structure is of a tuberculoid character show no higher degree of sensitivity to tuberculin than the nontuberculoid types.

#### COMMENT

It appears that there is a decided difference in the results obtained in fresh and in long-standing infections of leishmaniasis, this is particularly obvious in recurrent leishmaniasis as well as in the variants forming the transition to the recurrent type.

There remains the question as to what conclusions we are allowed to draw from this increased sensitivity as long as the mechanism of the intracutaneous test is so little clarified. There seems to be no doubt that no parallelism need exist between sensitivity and immunity. That the individual patient, particularly with recurrent leishmaniasis, may show certain fluctuations so that the result of the test may be negative even in any concentration is only evidence of peculiar reactions taking place in the organism, with no spontaneous healing of leishmaniasis.

From the foregoing it appears that recurrent leishmaniasis would have to be imagined to represent an extremely allergic type (similar to the papulonecrotic tuberculid in tuberculosis of the skin [Bonnievie and Bjørnstad<sup>6</sup>]).

From table 1 it is further seen that in part of the cases the reaction was still positive with dilutions in which no parasites were present. Although with reference to a dilution 1:1,000,000 this cannot be maintained with absolute certainty, since there is always the possibility of technical mistakes, there can be no doubt that the dilution 1:10,000,000 is actually free from parasites. Two patients with recurrent leishmaniasis still yielded a distinctly positive reaction with this dilution. This leads one to the question as to whether the leishmania parasite is able to produce any kind of toxin and whether the positive reaction would represent a response to its activity.

## SUMMARY

Eighty-four patients presenting leishmaniasis nodosa and leishmaniasis recidiva received graded doses of leishmania vaccine intracutaneously

The response to the graded intracutaneous doses of the vaccine varies in degree for the different types of the disease. The fresh nodular types are those most frequently showing a positive response to dilutions of the vaccine of 1:100 to 1:10,000 (normergic zone). Recurrences and early forms with lymphogenic spread display reactions on a much higher average level, the maximum lying between 1:10,000 and 1:10,000,000 (hyperergic zone).

This goes to prove that the recurrent types of leishmaniasis have a more pronounced allergic component. These graded intracutaneous tests may possibly be of importance in the recognition of early infections tending to develop into the recurrent form.

The response to graded doses shows no parallelism to the number and severity of lesions.

## SYSTEMIC TREATMENT OF CREEPING ERUPTION

J M HITCH, MD\*

RALEIGH, N C

IN THE time-honored but, unfortunately, always awkward and frequently unsatisfactory treatment of larva migrans as encountered in this country, various physical and chemical local applications have been employed. Since the classic delineation of this condition as seen in the southeastern United States by Kirby-Smith, Dove and White<sup>1</sup> in 1926, there had been no radical changes in its therapy until D C Smith<sup>2</sup> introduced the use of fuadin in 1943. Following this real advance in therapeutics, reports have appeared which in the main substantiate the observation that this antimony compound is in many instances toxic for the larva (Wilson<sup>3</sup> and Rubin<sup>4</sup>). However, some investigators have found that the medicament is frequently ineffective in completely eradicating the infestation (Blank<sup>5</sup> and Dolce and Franklin<sup>6</sup>). Recently Hailey and Hailey<sup>7</sup> reverted to local therapy after becoming discouraged with the use of fuadin systemically and reported cures with the application of onion poultice.

Early in the summer of 1945 it became evident that larva migrans would be fairly prevalent in the southeastern United States. Because the efficacy of the various forms of treatment is a moot question, it was decided to study the problem by extending the investigation to other drugs and to tabulate the various factors in each case in an effort to account for the success or failure of each medicament.

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This article has been released for publication by the Division of Publications of the Bureau of Medicine and Surgery of the United States Navy. The opinions and views set forth in this article are those of the writer and are not to be construed as reflecting the policies of the Navy Department.

1 Kirby-Smith, J L, Dove, W E, and White, G F. Creeping Eruption, *Arch Dermat & Syph* **13** 137 (Feb) 1926.

2 Smith, D C. Treatment of Creeping Eruption with Sodium Antimony Biscatechol (Fuadin), *J A M A* **123** 694 (Nov 13) 1943.

3 Wilson, J F. Treatment of Creeping Eruption with Fuadin, *J Florida M A* **30** 425 (April) 1944.

4 Rubin, S S. Creeping Eruption, *J A M A* **124** 668 (March 4) 1944.

5 Blank, H. Use of Fuadin in Creeping Eruption, *J A M A* **123** 989 (Dec 11) 1943.

6 Dolce, F A, and Franklin, J E. Creeping Eruption, *Arch Dermat & Syph* **52** 174 (Sept) 1945.

7 Hailey, H. Treatment of Creeping Eruption (Larva Migrans), *South M J* **39** 371 (May) 1946.

From July to December approximately 40 cases were seen, of which 33 are used in whole or in part in this report. All these cases were observed at a naval hospital serving a large Marine base in southeastern North Carolina. This region is sandy and during the period of this observation was subjected to excessive rainfall. A few of the patients were servicemen, who were hospitalized, but the majority were minor dependents, living nearby and seen as outpatients. The residence of these outpatients was largely from two sections: the first, a wartime housing project, which, though planted, still has much bare sandy soil, and, the second, a "trailer camp," which offers only deep sand in which the children can engage in outdoor play. Both of these residential areas are heavily populated by dogs and cats, many of which are strays because of the rapid turnover of personnel.

In the period when most of these cases were being observed, several stray and attended dogs and cats from the localities concerned were examined for intestinal parasites. *Ankylostoma braziliense* ova were almost universally present, but no other parasites or ova were found. This observation was corroborated, in the main, by the veterinarians at the nearby Marine War Dog Training School. Since no other source of infestation was obvious and the clinical picture and local conditions were practically identical with those in the classic descriptions of Kirby-Smith, Dove and White,<sup>1</sup> White and Dove<sup>8</sup> and Shelmire,<sup>9</sup> it was felt that it was justified to assume that the patients were suffering from infestation with the third stage larvae of *Ankylostoma braziliense*.

#### CLINICAL AND LABORATORY DATA

As mentioned previously, there were 33 patients from whom sufficient information was obtained to warrant inclusion of some phase of their study or treatment in this report. Five of these patients had definite clinical evidence of reinfestation following cure, and these cases are considered separately. Nine were young adults and the remainder children between the ages of 1 and 7 years, with the preponderance of patients in the second to fourth years. The studies made failed to reveal any significant difference between the age groups as regards the physiologic response to this infestation or therapeutic results (table 1).

In this group, lesions were observed on all portions of the body except the head. There were, of course, more lesions on the feet than elsewhere. The number of active larvae ranged from one to considerably more than a hundred on a single patient. Neither the location of the eruption nor the number of lesions seemed to affect response to treat-

<sup>1</sup> White, G. F., and Dove, W. E. The Causation of Creeping Eruption, J. A. M. A. **90** 1701 (May 26) 1928.

<sup>9</sup> Shelmire, J. B. Experimental Creeping Eruption from a Cat and Dog Hookworm (*A. Braziliense*), J. A. M. A. **91** 938 (Sept. 29) 1928.

ment or influence the laboratory findings except possibly in 2 adult patients, who, having approximately sixty and one hundred active larvae, showed a relative eosinophilia of 32 and 22 per cent respectively. These were the highest eosinophilias observed, though several patients with few lesions exhibited striking increases in eosinophil count (table 1).

The time between the first observation of the disease and initiation of treatment varied between one and thirty days but seemed to have no bearing on the outcome.

TABLE 1—*Results of Examination of Patients with Creeping Eruption*

Patient *	Number of Larvae	Duration, Days	White Blood Cells	Eosinophils, %	Fall in Sedimentation Rate in 1 Hr., Mm
1		3	6,750	0	12
2	100	22	6,800	22 10 3	2 5
3	60	30	11,200	32 5	19 6
4		2	11,650	10	20
5		2	12,550	4	10
6	4	10	7,300	19 4	13 4
7	1		7,800	6	10
8	1	7	9,000	0	21
9		3	16,000	2	9
10	8	5	13,100	2	
11	1	2			
12	2	4	7,000	6	10
13	2	1	4,800	0	10
14	1	9	9,250	8	9
15	1	2	6,250	5	10
16	1	3	12,750	0	15
17	1	1	8,000	12	9
18	1	30	10,850	3	10
19	1	30	9,200	8	
20	2	4	7,650	7	
21	1	7	10,150	2	15
22			8,000	6	15
23	5	4	6,600	3	14
24	6	10	11,800	18	14
25		3	8,700	16	6
26	100	10	8,900	2	
27	8	10	7,900	2	7
28	4	21	8,400	0	11
29			9,600	3	
30	1	2			
31	5				
32					
33	30	30	10,200	17	

\* The patients numbers assigned here remain constant in the tables following

Routine studies of the elements of the blood failed to show any significant effect on the red cells. In the 26 patients in whom this factor was determined, the erythrocyte count varied from 3,350,000, with a hemoglobin content of 53 per cent (an obviously chronically anemic child), to 5,350,000, with a hemoglobin content of 97 per cent. An average reveals a red cell count of 4,220,000 and hemoglobin content of 77 per cent. On the other hand, the same number of patients showed a definite tendency to mild leukocytosis. White cell counts ranged from 4,800 to 16,000, with an average of 9,272. Differential counts showed no appreciable alteration in the relationship of the various elements

except for eosinophilia, which in a few cases was considerable. Shelmire<sup>9</sup> and Wright and Gold,<sup>10</sup> among others, have found this also. These counts were usually obtained on the patient's first visit, but, since the duration of the disease at the time of the patient's initial visit varied widely, the cell counts and differentials would seem to reflect a fair cross section of the leukocytic response during the active phase of the disease. The eosinophil counts ranged from 0 to 32 per cent, with an average of 7 per cent. As previously mentioned, the highest eosinophilia (case 3—32 per cent of 11,250 white blood cells) was obtained in a hospitalized adult patient who presented approximately sixty larval burrows. With clinical improvement following treatment this eosinophilia dropped to 5 per cent. Another adult patient (case 2), with more than one hundred active lesions, revealed an eosinophilia of 22 per cent, but with the patient under therapy the eosinophil count subsequently returned to normal (table 1).

Apparently infestation with *Ankylostoma braziliense* is capable of producing an increase in the erythrocyte sedimentation rate, though no correlation between the speed of sedimentation and the severity of infestation could be found. The adult patient with sixty larvae, previously referred to, had a sedimentation rate of 19 mm in one hour. On the other hand, the adult patient with more than one hundred active lesions showed a sedimentation rate of only 5 mm in one hour. In twenty-four determinations of the erythrocyte sedimentation rate the values ranged from 2 to 21, with an average fall of 11.5 mm in one hour. Despite the known volatile character of this test in children, it is felt that the findings in this group justify the conclusion that infestation with *Ankylostoma braziliense* causes a moderate increase of the sedimentation rate (table 1). This finding is at variance with that of Wright and Gold,<sup>10</sup> who demonstrated normal rates in patients with *larva migrans* except for 1 patient who had concomitant cellulitis.

The stools of 12 patients were examined for ova and parasites. In none of these was *Ankylostoma braziliense* found. In 3 the results were positive for other intestinal parasites, viz., *Iodamoeba buetschlii*, *Endamoeba coli* and *Giardia lamblia*. This finding follows many of the previous observations<sup>11</sup> that the dog and cat hookworm as encountered in this section is not an intestinal parasite for human beings.

Since Wright and Gold<sup>10</sup> recently recounted the roentgenographic demonstration of a pulmonary infiltration as a concomitant pathologic change in creeping eruption, roentgenograms of the chest were obtained in 13 of these patients. All were negative for any type of pulmonary

10 Wright, D. O., and Gold, E. M. Loeffler's Syndrome Associated with Creeping Eruption, *J. A. M. A.* **128**: 1082 (Aug. 11) 1945.

11 Kirby-Smith, Dove and White.<sup>1</sup> Shelmire.<sup>9</sup> Wright and Gold.<sup>10</sup>

abnormality Wright and Gold reported that the changes were migratory and transient, and they obtained serial studies in their 9 cases with pulmonary infiltration. In the patients presented here repeated roentgenologic examinations of a single patient were not obtained, but in consideration of the entire group, roentgenograms were examined which were made from the third to seventy-second day of the disease.

#### TREATMENT

Four drugs were used in the systemic treatment of this group of patients. These were fuadin, neostibosan (diethylamine para-aminophenylstibinate), antimony and potassium tartrate and oxophenarsine hydrochloride. All were used with the emphasis on the clinical approach. This, of course, leaves much to be desired when one is attempting to make a statistical assay of the results. Many factors appeared in the study to vitiate a clear picture of the outcome. The chief one of them was the large number of patients lost from observation as a result of military transfer of the fathers. Others were occasional lack of cooperation, difficulty in continuing the administration of a certain drug (e g, intravenous administration in small children or nausea) and the accurate determination of cure. This last factor is of considerable importance in the evaluation of any treatment for creeping eruption. Long periods of dormancy have been reported by Rigdon<sup>12</sup> and others, and there is no test other than clinical observation to verify the results of therapy. All the patients presented here were observed for at least several weeks following the last treatment before a satisfactory outcome was assumed. In no case was reinfection diagnosed if there was any reasonable doubt as to the previous cure. In the tabulation and discussion of the results with the various drugs used, no reference is made to the patient's age, number and location of the larvae or the laboratory findings, since none of these seemed to influence the outcome.

*Fuadin (Sodium Antimony III Bis-catechol-2,4 Disulfonate)* — Fuadin was given either originally or after another drug which had been discontinued because of failure or difficulty with continued administration. The dosage was 50 cc intramuscularly in adults and a proportionate amount based on age and size in children. In general, the 2 to 4 year old patients received 1 to 1.5 cc. Injections were usually given every day or every other day. In all, 17 patients received fuadin.

Table 2 shows that in several instances this antimony compound was probably not given an adequate trial before treatment was changed. On the other hand, several patients received more than ten injections without cure while others experienced definite satisfactory outcome.

12 Rigdon, R. H. Creeping Eruption (Ankylostoma Braziliense Infestation) with Spontaneous Remissions and Recurrences, J. Pediat 16 637 (May) 1940.

with but few doses of fuadin one with two injections totaling 30 cc (case 1) With the scheme of treatment used, cures were demonstrated in slightly less than half the cases adequately followed (table 2)

*Neostibosan* (*Diethylamine Para-Aminophenylstibimate*) Since treatment with fuadin did not seem entirely satisfactory, it was decided to compare the clinical response with other antimony compounds So far, two of these have been used (*neostibosan* and antimony and potassium tartrate) In neither was precedent in dosage for this type of disease available, and it is appreciated that larger doses may have proved more efficacious Roughly, adults received 0.15 and 0.2 Gm and small children (2 to 4 years of age) 0.05 Gm of *neostibosan*, with intermediate

TABLE 2—Results with Fuadin

Patient *	Previous Treatment	No of Injections	Total, Gm	Time, Days	Outcome †
3	None	23	111.5	30	Change to neostibosan
6	None	8	36.5	8	Change to neostibosan
7	None	5	5.0	7	Change to neostibosan
10	Neostibosan (× 3)	19	19.0	21	Change to oxophenarsine hydrochloride
13	Neostibosan (× 8)	2	2.0	3	Change to oxophenarsine hydrochloride
33	Oxophenarsine hydrochloride (× 3)	13	16.0	20	Change to local therapy
4	None	2	3.0	2	Unknown
5	None	4	5.0	18	Unknown
11	None	10	14.5	20	Unknown
18	None	2	2.0	3	Unknown
19	None	6	6.0	9	Unknown
20	None	5	6.5	6	Unknown
1	None	2	3.0	2	Cured
2	None	15	71.5	25	Cured
9	None	8	6.3	17	Cured
17	Antimony and potassium tartrate (× 1)	4	6.0	4	Cured
25	Oxophenarsine hydrochloride (× 9)	4	3.0	8	Cured

\* Total cases 17

† Results of treatment were as follows: cured 5, unknown 6 and failure 6

ages in proportion, every day or every other day All injections were given intravenously except to the patients in cases 3 and 8, who received two intramuscular injections each This method of administration was abandoned because of severe pain Table 3 shows the results with *neostibosan* used in 10 cases

It is evident that results with this drug were highly inconsistent Preceding fuadin treatment seemed to have no effect on the outcome The 3 patients cured with *neostibosan* had no previous therapy, yet they experienced complete relief with few injections (cases 8, 12 and 16) A hypothesis that fuadin and *neostibosan* are chemically antagonistic seems untenable, particularly since in these cases several days elapsed between administration of the two drugs In contradistinction to the patients cured with a minimal number of injections, attention is called to a patient (case 14) who received twelve injections without

demonstrable benefit Though the number of patients treated with this drug is small, it appears that the results are of about the same order as those obtained with fuadin (37 vs 45 per cent of cures in cases followed)

*Antimony and Potassium Tartrate*—Antimony and potassium tartrate was given to only 2 patients One adult received doses of approximately 0.1 Gm and 1 child 0.01 Gm intravenously The results appear in table 4

TABLE 3—Results with Neostibosan

Patient *	Previous Treatment	No of Injections	Total, Gm	Time, Days	Outcome †
3	Fuadin (× 23)	3	0.65	3	Change to antimony and potassium tartrate
6	Fuadin (× 8)	3	0.80	10	Change to oxophenarsine hydrochloride
10	Fuadin (× 6)	3	0.20	3	Change to fuadin
13	None	8	1.10	14	Change to fuadin
14	None	12	1.75	16	Change to oxophenarsine hydrochloride
7	Fuadin (× 5)	1	0.05	1	Unknown
15	None	5	0.95	7	Unknown
8	None	2	0.30	2	Cured
12	None	2	0.35	6	Cured
16	None	1	0.2	1	Cured

\* Total cases 10

† Results of treatment were as follows: cured 3, unknown 2 and failure 5

TABLE 4—Results with Antimony and Potassium Tartrate

Patient *	Previous Treatment	No of Injections	Total, Gm	Time, Days	Outcome †
3	Fuadin (× 13), neostibosan (× 3)	8	0.75	1	Cured
17	None	1	0.01	1	Vomiting; change to fuadin

\* Total cases 2

† Results of treatment were as follows: cured 1 and failure 1

It is felt that no conclusions can be drawn from these 2 cases The patient in case 3, with approximately sixty larvae, had been infested for fifty-six days and received appreciable other antimony therapy before antimony and potassium tartrate was given It is possible that the age of the larvae and the toxicity of the previous antimony preparation aided in their destruction

In both cases nausea was great, and in case 17 severe vomiting precluded the further use of this drug

*Oxophenarsine Hydrochloride* Since the treatment of larva migrans with the three available antimony compounds had not proved wholly satisfactory, it was decided to investigate the effects of a similar chemical—arsenic on this infestation This study was begun in August 1945

and oxophenarsine hydrochloride has been the only compound investigated to date

An effort was made to administer a treatment every three to five days, and in all instances the drug was given intravenously. Adults usually received 0.06 Gm and children a smaller dose, based roughly on size. The 2 to 4 year old patients usually were given 0.015 Gm. A total of 17 patients were treated with this method.

It is seen that the results with oxophenarsine hydrochloride, which appear in table 5, are somewhat superior to those obtained with the antimony compounds. In this series 63 per cent of cures were obtained in the cases adequately observed. Again previous antimony therapy did not seem to alter the outcome.

TABLE 5—*Results with Oxophenarsine Hydrochloride*

Patient *	Previous Treatment	No of Injections	Total, Gm	Time, Days	Outcome †
25	None	9	0.135	28	Change to fuadin
33	None	3	0.035	8	Change to fuadin
26	None	5	0.070	13	Failed
27	None	2	0.100	3	Failed
28	None	7	0.280	28	Failed
10	Fuadin (× 19), neostibosan (× 3)	2	0.015	5	Unknown
22	None	2	0.030	3	Unknown
29	None	2	0.030	3	Unknown
31	None	1	0.015	1	Unknown
6	Fuadin (× 8), neostibosan (× 3)	2	0.120	2	Cured
13	Neostibosan (× 8), fuadin (× 2)	2	0.025	12	Cured
14	Neostibosan (× 12)	2	0.030	6	Cured
21	None	1	0.020	1	Cured
23	None	8	0.260	54	Cured
24	None	9	0.114	49	Cured
30	None	3	0.050	8	Cured
32	None	4	0.080	12	Cured

\* Total cases 17

† Results of treatment were as follows: cured 8, unknown 4 and failure 5

There were no severe reactions to the drug, and only 1 patient (case 33) experienced vomiting.

#### COMMENT

Adequate evaluation of any new form of treatment requires much more extensive clinical trials than those presented in this report. However, it is felt that the publication of this material is justified because no large series of cases of larva migrans has been presented since the introduction of systemic treatment with fuadin in 1943.

Notwithstanding conflicting reports on the efficacy of fuadin in infestation of human beings with *Ankylostoma braziliense*, there is no doubt that in certain cases it is larvicidal. In about the same proportion of cases neostibosan proved satisfactory in this small series. The other antimony compound employed, antimony and potassium tartrate, was used in only 2 cases. In 1 of these, use of it was discontinued after one injection because of vomiting, and in the other the patient had an

old infestation and had received much previous treatment. Therefore no conclusions can be drawn relative to this drug.

The first few patients in whom arsenic in the form of oxophenarsine hydrochloride was employed responded rapidly, and for a considerable period it was felt that a perfect remedy had been discovered. However, further observation of these patients and succeeding patients considerably dimmed this view. I first mentioned the successful use of oxophenarsine hydrochloride and its limitations in discussing Hailey and Hailey's paper on larva migrans presented at the meeting of the Southern Medical Association in November 1945<sup>13</sup>. Now, after an adequate follow-up period, it appears that oxophenarsine hydrochloride is at least slightly superior to the antimony compounds as a larvicide in *Ankylostoma braziliense* infestation.

In the group of cases reported here the juggling from one drug to another, with perhaps resultant inadequate dosages, undoubtedly vitiates the results. However, since all the medicaments were employed in essentially the same manner, comparison appears justified.

Relief from pruritus and temporary cessation of migration, often in a few hours, with both antimony and arsenic compounds bears adequate testimony to the larvostatic properties of all of them. The clinical impression was that this is somewhat commoner with oxophenarsine hydrochloride.

The lack of correlation between the severity or duration of the disease and its response to treatment is disturbing and unexplained. Similarly, the absence of parallelism between amounts of drug used, whether singly or in combination, and cure is inexplicable. However, the possibility of greater efficacy by a great increase of the dosage, principally by more frequent injections, seems worthy of consideration. This appears particularly applicable in the case of a rapidly eliminated drug given intravenously such as oxophenarsine hydrochloride. Since this group of patients was largely composed of small children, such procedures were not deemed advisable.

A comparison of the various drugs used in this study indicates that the arsenical is slightly superior as a larvicide, on the average it effects cures with less frequent and fewer injections than fuadin and with less frequent treatments than neostibosan. Fuadin enjoys the distinct advantage of mode of administration, particularly in dealing with small children. Intramuscular administration of neostibosan causes far too much discomfort, though intravenously it seems reasonably free of undesirable reactions. Gastrointestinal upsets in the limited number of cases in which antimony and potassium tartrate was used were far too great to justify its use for such a benign disease.

13 Hitch, J. M., in discussion on Hailey and Hailey.<sup>7</sup>

Since the various local treatments of larva migrans are far from satisfactory and evidence is at hand that both antimony and arsenic used systemically are frequently larvicidal, a further investigation of these and perhaps other chemicals is definitely indicated

#### SUMMARY

Thirty-three cases of classic larva migrans presumably caused by *Ankylostoma braziliense* and observed at a military establishment in southeastern North Carolina during the summer of 1945 are presented

No correlation between age of the patient, duration of the disease or number of infesting larvae and course of the disease could be demonstrated

The larva apparently does not produce anemia

A moderate leukocytosis with eosinophilia and increase in the sedimentation rate usually accompanies this infestation

A concomitant pulmonary infiltration was not demonstrated

No evidence of migration of the larva to the intestinal tract was found

Larvostatic and larvicidal properties of both antimony and arsenic compounds were definitely demonstrated

Fuadin, neostibosan, antimony and potassium tartrate and oxophenarsine hydrochloride were used systemically. Cures were obtained in from 37 to 63 per cent with these compounds. The evidence at hand indicates that oxophenarsine hydrochloride is probably superior to the others employed for this disease

# MORBUS MONILIFORMIS LICHENOIDES

## Variant Types

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IT IS my purpose in this paper to review 3 cases of lichenoid lesions of the skin which more or less come under the heading of lichen ruber moniliformis or morbus moniliformis lichenoides. The first case I have studied in detail, the second case I had the opportunity to observe periodically for several years, and mention is made of a third case, which has been reported by Wise and Rein, by way of comparison.

Since Erasmus Wilson's first description of lichen planus in 1869, many clinical variations of this disease have been described. These include the well known hypertrophic, atrophic, linear, annular, bullous and erythematous types. In addition to these, various cases have been reported in the literature from time to time which do not exactly fit in with the picture of lichen planus either clinically or histologically. Ormsby<sup>1</sup> in 1910 reported a group of 6 cases of lichen sclerosus in which he felt that the conditions were forms of lichen planus.

Nomland<sup>2</sup> in 1930 reported a series of cases of lichen sclerosus et atrophicus and white spot disease which were interpreted as being essentially different from lichen planus. In 1940 Montgomery<sup>3</sup> published a paper on lichen sclerosus et atrophicus, maintaining that this disease was hydropic and degenerative in character and was distinctive from atrophic lichen planus, on the one hand, and guttate morphea, on the other. In 1886 Kaposi<sup>4</sup> reported the case of an atypical lichenoid disease, to which he gave the name lichen ruber moniliformis. He stated the belief, however, that it was a form of lichen planus. In 1936 Wise and Rein<sup>5</sup> reviewed 16 reported cases of lichen ruber moniliformis and also reported a case of their own. This case they felt was

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1 Ormsby, O. Lichen Planus Sclerosus et Atrophicus (A Report of Six Cases with a Review of the Literature), *J. A. M. A.* **40** 901 (Sept. 10) 1910.

2 Nomland, R. Lichen Sclerosus et Atrophicus (Halo-peau) and Related Cutaneous Atrophies, *Arch. Dermat. & Syph.* **21** 575 (April) 1930.

3 Montgomery, H., and Hill, W. R. Lichen Sclerosus et Atrophicus, *Arch. Dermat. & Syph.* **42** 755 (Nov.) 1940.

4 Kaposi, M. Lichen Ruber Moniliformis, *Vierteljahrsschr. f. Dermat.* **13** 571, 1886.

5 Wise, F., and Rein, C. R. Lichen Ruber Moniliformis (Morbus Moniliformis Lichenoides), *Arch. Dermat. & Syph.* **34** 830 (Nov.) 1936.

similar to the one originally reported by Kaposi, but they interpreted it differently. They felt that the clinical and histologic picture was inconsistent with that of lichen planus and that it should be considered a disease *suu generis*.

They suggested the name morbus moniliformis lichenoides. They felt that the following points justified the establishing of this new entity: (1) the clinical picture, which consisted of a bizarre arrangement of waxy papules, nodules and keloid-like, elongated strands, forming parallel ridges chiefly on the neck and flexor surfaces of the arms and legs and disposed in conspicuous vertical rows corresponding to the long axes of the neck and extremities, (2) histologic changes characteristic of lichen planus not observed, the essential pathologic changes being vasculitis and perivasculitis with degenerative changes in the corium, and (3) lack of response to therapy for lichen planus and no tendency to spontaneous recovery.

I should agree with Wise and Rein in their interpretation of their case and of the case reported by Kaposi.

#### REPORT OF CASES

CASE 1—Sister X first consulted me in July 1941. She was a 33 year old nun. She stated that in December 1940, a rash had developed on her back and chest. The onset was rather sudden, the lesions reaching approximately their present appearance in about two weeks' time. Since then there has been no tendency either to spread or to regress. Examination showed two types of lesions, a lichenoid type and an urticarial type. The lichenoid type consisted of dusky yellowish papules and nodules of from 1 to 4 mm in diameter. Some of the larger nodules gave the impression of being rather translucent, with a slight yellowish tinge. They were firm on pressure. They were dome shaped and showed no umbilication or polygonal contour. There was no inflammatory reaction at the base and no tendency to scaling, the surface being smooth and shiny. As to distribution, the denser areas were on the chest and on the back, between the shoulders and extending in a V shape almost to the waist. On the arms and deltoid region the lesions were moderately dense, becoming less so toward the wrists and hands, where only a few scattered lesions were found. The flexor surfaces were comparatively free. A few small lesions were found above the right eyebrow, otherwise the face was clear. The mucous membranes were not involved, and no lesions were present below the waist or on the legs or feet. There were no excoriations, and the patient stated that there was no itching or burning from these papular lesions.

The urticarial lesions were of an annular and arciform type. Some were small, but most of them were 4 to 6 inches (10 to 15 cm) in diameter. They were somewhat fugacious, although some lesions were observed which existed for several days. They gave one the impression of erythema multiforme or erythema perstans. These urticarial lesions itched intensely in contrast to the papular lesions and were observed to come on all parts of the body from time to time. She had never been free from these lesions for more than three or four days at a time since the onset.

A general medical examination carried out at St Mary's Hospital was essentially noncontributory. The patient was well nourished, had no complaints and seemed to be in the best of health. There was no evidence of sinus infection, her tonsils had been removed and the throat showed no congestion. The teeth were in good condition, and dental roentgenograms showed no pathologic changes. Examination of the chest, abdomen and extremities showed nothing abnormal. There was no evidence of arthritis, and there had been no complaints of either muscular pain or pain in the joints. She was a member of a large family, and no other member of the family had had any similar trouble.

*Laboratory Studies*—The blood cell count showed 4,500,000 red cells and 90 per cent hemoglobin. The white cell count showed 6,800 cells. The differential count



Fig 1 (case 1) —Cutaneous lesions of Sister X

was as follows: polymorphonuclear leukocytes 42 per cent, lymphocytes 48 per cent, monocytes 2 per cent, eosinophils 4 per cent and myelocytes 4 per cent. The Wassermann reaction was negative. Culture of the blood showed no growth. Studies of the blood fat, done by the pathology department of St Mary's Hospital, gave results as follows: total cholesterol content 50 mg per hundred cubic centimeters, total fatty acid content 90 mg and total lipid content 148 mg. These values are lower than normal, but whether they are of any significance is difficult to say. The urine contained no sugar, albumin, casts or red or white cells. The specific gravity was 1.020. A determination of the blood sugar content gave a value of 120 mg. One of the nodules was removed aseptically and was cultured aerobically by the pathologist. No growth was obtained after three weeks. In order to rule out a diagnosis of amyloid disease, injection about the lesions was made with 1 per cent congo red. The nodules did not absorb any of the dye.

Two biopsies were performed. One specimen of a flat lesion which seemed to be inactive was submitted to Dr. Herbert Brown, pathologist, who reported some slight acanthosis, round cell infiltration about blood vessels of the corium with thickening of the vessel walls and some degeneration of the collagen in deeper areas.

A second biopsy specimen, of a large active-appearing lesion, was taken and sent to Dr. Fred Weidman for examination. His report is as follows: "Microscopically the reaction is found to be a polymorphonuclear perivascular one. This at once brings into consideration conditions which have as their basis a factor such as that concerned in rheumatism. It is an outside possibility that

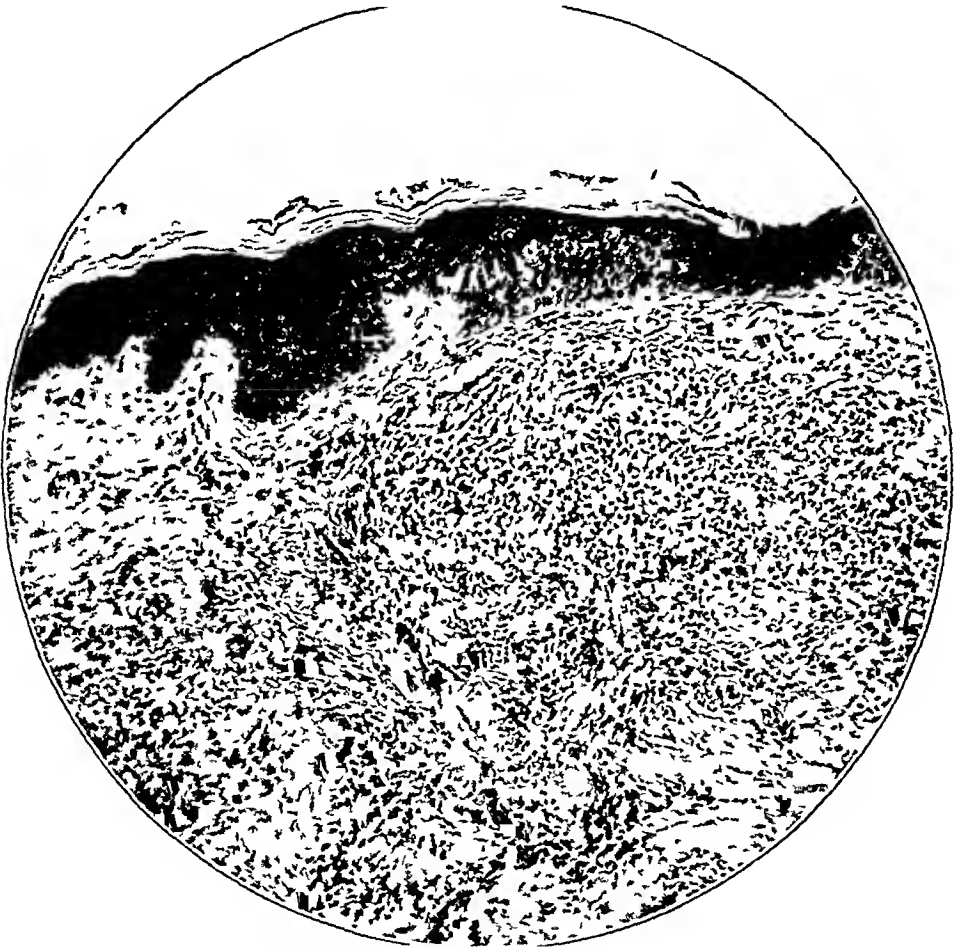


Fig. 2 (case 1) —Section under low power magnification, showing perivascular infiltration of lymphocytes and polymorphonuclear cells, edema, collagenous degeneration and necrosis with some attempt at regeneration.

it is periarteritis nodosa. More likely these are closely related to rheumatic nodules, although the distribution is not exactly right for that. Xanthomatous conditions can be definitely excluded, such as might be implied by the yellowish color observed clinically."

*Summary of Histologic Studies* —In the slide of the larger, more active lesion, the epidermis shows slight hyperkeratosis. The granular layer, prickle cell layer and basal layer show about normal relationship. Acanthosis is absent, and an area of pressure atrophy is present over the active lesion. The most obvious

pathologic change consists of a round, well circumscribed area of cellular infiltrate extending from immediately beneath the epidermis down deep into the corium. This area consists largely of polymorphonuclear cells with some round cells. The infiltrate is largely perivascular, and there is thickening of the blood vessel walls and some thromboses. Extensive edema and minute areas of necrobiosis are seen. A feeble attempt at regeneration of the connective tissue may be seen at the periphery. Elsewhere in the corium areas of collagenous degeneration are observed, in some places amounting to a homogeneous, basophilic mass.

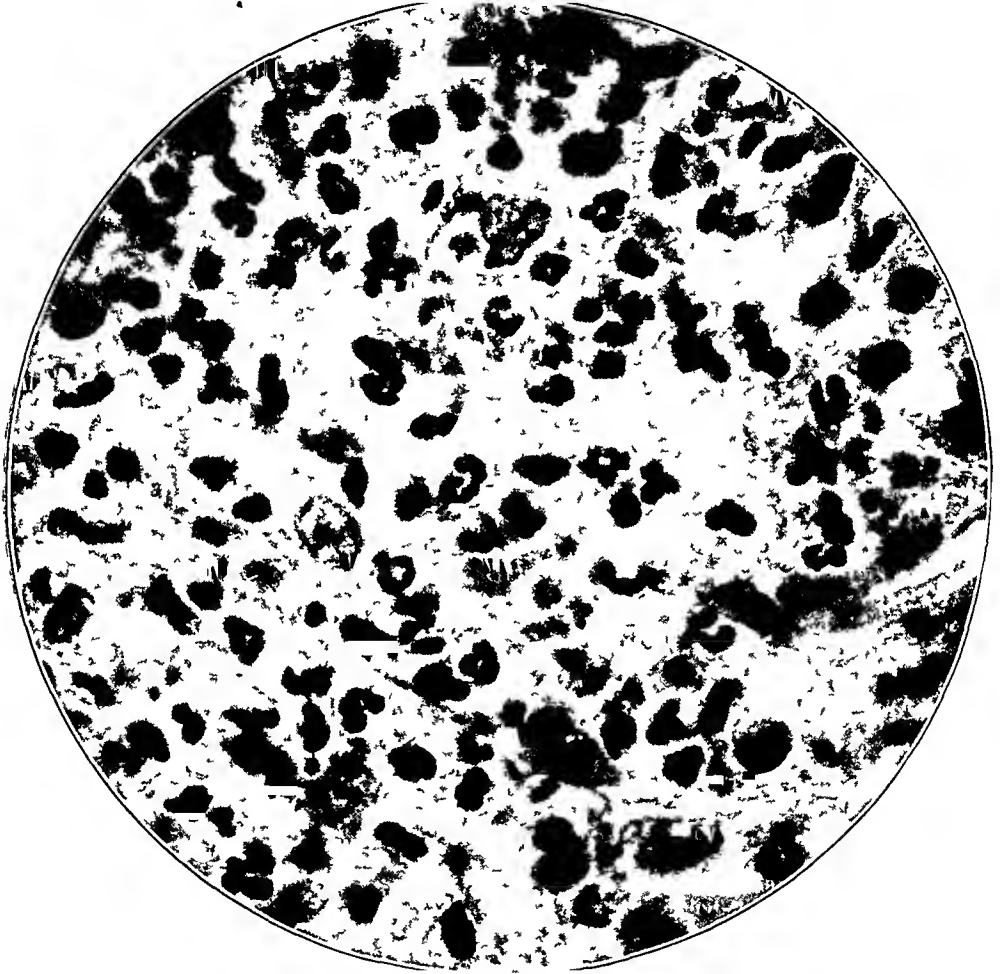


Fig 3 (case 1) —Section under high power magnification, showing polymorphonuclear infiltrate

The slide of the flat, more inactive lesion shows a slightly different picture, probably due to the age of the lesion. There is absence of the polymorphonuclear infiltrate and instead a moderate round cell infiltration about blood vessels. There is some degeneration of the collagen, and the epidermis shows moderate acanthosis.

A section stained with sudan III showed no excess extracellular fats. The photographs presented show the clinical appearance of the lesions and some of the histologic changes observed.

*Treatment*—No change in the clinical picture was obtained by the administration of eight roentgen ray treatments of 80r each at weekly intervals together with bismuth therapy. The patient was then given 75,000 units of vitamin A daily for a period of two months, without improvement. With the thought that the disorder might be due to some blood-borne infection, she was given 4 Gm of sulfadiazine daily for ten days. Neither the urticarial nor the lichenoid lesions were influenced by any of these procedures. Now, after an observation period of five years, her eruption is unchanged. She has no complaints except that she tires easily. The results of physical examination remain essentially normal.

CASE 2—Mr G, a man aged 50, was presented before the Buffalo-Rochester Dermatological Society in 1935. He showed a generalized lichenoid rash of about three years' duration. In spite of atypical pathologic changes and clinical course, a diagnosis of lichen planus was made by most of the members present. About a year later he was again presented at the same society, and this time the diagnosis of amyloid disease was suggested, because of the progressive thickening and lardaceous character of the skin. However, a congo red test performed elicited a negative reaction. In 1936 the patient was presented at the Central States Dermatological Association at Cleveland. Several of the pathologists at that time felt that the microscopic picture was at least compatible with the diagnosis of lichen ruber moniliformis or morbus moniliformis lichenoides. Later, sclerodermatous changes developed, with typical sclerodactylia, firmness of subcutaneous tissues of the trunk and extremities and sclerotic changes in the face, producing a masklike expression and great limitation of ability to open the mouth. He died two years later of malnutrition and changes incidental to his generalized progressive scleroderma.

CASE 3—The third case I wish to refer to is that reported by Wise and Rein<sup>6</sup> in 1936. In a personal communication Dr Wise told me that this patient died of cardiac disease at the age of 38. The autopsy revealed nothing of significance except in the heart. This may or may not be significant, as I do not have details of the autopsy, but it is at least suggestive of a possible relationship between the cutaneous lesions and vascular disease in so young a patient.

In comparison with this case of Wise and Rein, I would call attention to the following variations in case 1 and case 2. First, the patient in case 1 showed a rather uniform distribution of lesions and did not have the parallel bands or linear beadlike arrangement described by Kaposi and by Wise and Rein. Second, the lesions were confined to areas above the waist and were not generalized, as were those in case 2 and in that of Wise and Rein. Also, the lesions were more on the extensor than on the flexor surfaces. Third, the patient in case 1 had accompanying large, annular, erythema multiforme-like lesions, which were not found in the previous cases.

Fourth, the histologic structure in this case showed, in addition to the degenerative changes before described, massive polymorphonuclear areas of infiltration. This was not noted in the case of Wise and Rein and may represent simply an early active stage of the disease.

As to case 2, there is the unusual complication of a superimposed extensive and fatal scleroderma.

## DIFFERENTIAL DIAGNOSIS

*Lichen Planus*—While there was a superficial resemblance of the lesions in cases 1 and 2 to lichen planus, yet on closer examination they were not at all similar. They lacked the polygonal shiny-topped character usually seen and the purplish hue. The histologic picture was also different and showed none of the changes usually seen in lichen planus.

*Xanthomatosis*—Knowledge of the xanthomas has been greatly clarified in recent years by various investigators, especially by Montgomery and his associates<sup>6</sup> and by Laymon.<sup>7</sup> These studies include details of histopathology and of lipid metabolism. In cases 1 and 2 there were no xanthoma cells, no evidence of extracellular cholesterosis and nothing in the studies of blood fat to suggest a disturbance of fat metabolism.

*Amyloidosis*—In both cases the congo red test elicited no reaction characteristic of amyloid infiltration. Clinically, there was a lack of the thickened, patchy, pruritic type of lesion usually seen in amyloid disease.

*The Rheumatic Diseases*—From a purely histologic viewpoint, in case 1 the changes were similar to those in the group which Weidman prefers to call the rheumatic diseases. The pathologic changes consist essentially of vasculitis and perivascularitis, as evidenced by leukocytic infiltration and thickening of vessel walls, tendency to thrombosis and secondary degenerative changes such as collagenous degeneration, edema, necrobiosis and some regeneration of connective tissue. Changes of this type are found in varying degree in the following clinical entities: rheumatic nodule, periarteritis nodosa, dermatomyositis, lupus erythematosus, scleroderma, erythema nodosum and erythema elevatum diutinum. For a more detailed discussion of these diseases, reference is made to articles by Coates and Coombs,<sup>8</sup> Weidman and Besancon<sup>9</sup> and Trimble.<sup>10</sup>

6 Montgomery, H. Cutaneous Manifestations of Lipoid Metabolism, *M. Clin. North America* **24** 1249 (July) 1940. Montgomery, H., and Osterberg, A. E. Xanthomatosis, *Arch. Dermat. & Syph.* **37** 373 (March) 1938. Montgomery, H., and Havens, F. Z. Xanthomatosis, Lipoid Proteinosis (Phosphatid Lipoidosis), *Arch. Otolaryng.* **29** 650 (April) 1939. Hildebrand, A. G., Montgomery, H., and Rynearson, E. H. Necrobiosis Lipoidica Diabeticorum, *Arch. Int. Med.* **66** 851 (Oct.) 1940.

7 Laymon, C. W. Extracellular Cholesterosis, *Arch. Dermat. & Syph.* **35** 269 (Feb.) 1937.

8 Coates, V., and Coombs, C. F. Rheumatic Nodule, *Arch. Dis. Childhood* **1** 183 (Aug.) 1926.

9 Weidman, F., and Besancon, J. H. Erythema Elevatum Diutinum. Role of Streptococci and Relationship to Other Rheumatic Dermatoses, *Arch. Dermat. & Syph.* **20** 593 (Nov.) 1929.

10 Trimble, W. B. Erythema Elevatum Diutinum. Report of a Case with Remarks on Its Nosological Position, *Arch. Dermat. & Syph.* **13** 383 (March) 1926.

In view of the frequently seen tendency of the aforementioned diseases to overlap clinically and the similarity of basic vascular pathologic changes, it might not be going too far afield to keep in mind the possibility of a common etiologic agent, perhaps an agent such as is responsible for rheumatism. This rather bold suggestion is made with the hope of stimulating thought along the lines of basic pathologic changes and causation rather than on clinical appearances. Perhaps the term vasculitis or perivasculitis is as far as one can go at present. This basic pathologic change may be capable of producing a wide variety of clinical pictures.

#### SUMMARY

1 Two cases are reported of an atypical lichenoid eruption which probably fall into the class of morbus moniliformis lichenoides.

2 Variations are noted which differ from cases previously reported.

3 An essential vascular pathologic structure with secondary degenerative changes is noted, which seems to be a characteristic common to several other well known clinical entities.

4 It is suggested that a common etiologic factor may be present in this group of diseases such as is operative in rheumatism.

5 Serious or fatal complications may follow in the wake of vascular damage of this type.

277 Alexander Street

#### ABSTRACT OF DISCUSSION

DR FRED WISE, New York. Most dermatologists are still interested in unusual and bizarre eruptions, of which the subject of this paper is an example, despite the fact that morphologic dermatology is of relatively little importance when compared with experimental and research work.

The two forms of eruption described by Dr McFarland, while exhibiting certain features clinically similar to Kaposi's original lichen ruber moniliformis and to the eruption in the case described by Wise and Rein, are rightly designated as variants by the author. Most of the reported cases are also variants in relation to Kaposi's case. Some were aberrant examples of lichen planus, others showed no similarity in histologic structure to lichen planus.

In some of the cases the histologic changes have been regarded as suggestive of cutaneous eruptions associated with rheumatic disease. Dr Weidman, some ten years ago, as well as Dr Jacob, made this observation in their discussion of the case of Wise and Rein.

I should like briefly to recall to you the histologic changes in our case and to compare them with those in the case of Dr McFarland. In our case, in the early stage there was an exudative and inflammatory reaction in the upper part of the cutis, associated with degeneration of the vessel walls but without necrosis of any of the tissues or of the infiltrative elements. In the disease when it was at its height, the histologic picture showed intense degeneration and disintegration of tissue and of the cellular infiltrate, and in the final stage (we had an opportunity to take eleven biopsies) the deposition of connective tissue cells—possibly organizing tissue—replaced the parts which had broken down, so that

the process is evidently one in which vascular disease, as Dr McFarland emphasized—vasculitis—was associated with degenerative changes, and this was a predominant morbid change

In Kaposi's case there was a dense cellular infiltrate in the upper part of the corium and the cells were not characteristic of any particular type of dermatosis. There was no evidence of lichen planus.

In order to recall to you the appearance of a more characteristic moniliform eruption, I shall ask permission to show three slides. There is a typical arrangement of papules resembling a string of beads. Lesions are present which I compared with the hide of a Gila monster—beaded lesions but not actually moniliform in pattern. Vascular changes and absence of infiltration are demonstrated in the upper part of the corium, proving that in all stages there was not the slightest indication of lichen planus.

The histologic alterations in Dr McFarland's cases present features of similarity to other reported instances described as lichen ruber moniliformis, some of these are suggestive of the cutaneous lesions of periarteritis nodosa.

DR HIRAM E MILLER, San Francisco. I have a patient under my care who has an eruption similar to the one reported by Kaposi. Dr Wise stated that he thinks that Kaposi's case is unique. I believe that it is unique except for this 1 case that we have under our observation. In the 2 patients the location and type of the eruption and the pathologic changes are almost identical.

I agree with Dr Wise that the lichen ruber moniliformis described by Kaposi is entirely different from that presented by Dr McFarland this morning and different from that described by Dr Wise under the title of morbus moniliformis lichenoides. I might add that Nekam in 1938 described the same case that Kaposi had reported forty-three years before. While the two descriptions are of the same patient, Nekam's description is much more like that of our patient, because the eruption in both instances had been present for many years. You will recall that in Kaposi's report and in the subsequent description by Nekam the patient had an eruption on the face that somewhat resembled lupus erythematosus, a moniliform eruption on the extensor surfaces of the arms and forearms and keratotic lesions on the palms and soles.

This subject has been of considerable interest to me, and I had the findings in my patient ready for presentation at this time but it was decided that some other subject was more appropriate.

In regard to the pathologic changes, there is a bandlike infiltrate in Kaposi's patient and in the subsequent description of the same patient by Nekam. In that way, and in that way only, does it resemble lichen planus under the microscope.

DR ALBERT R MCFARLAND, Rochester, N Y. This paper was given the title, "Morbus Moniliformis Lichenoides. Variant Types," as it was realized that the clinical picture, at least, was somewhat different from that described by others, and yet the pathologic changes, clinical course and lack of response to treatment seemed to be consistent with this diagnosis. One hesitates to introduce a new name for a clinical picture purely on the basis of slight variations in the appearance of the gross lesions. I think that we all know that there can be considerable variation in the clinical appearance in the same disease. Whether or not this is a true variant of morbus moniliformis lichenoides or a somewhat new and different picture may be open to question.

# CLINICAL EXPERIENCE WITH AN OINTMENT OF SYNTHETIC COAL TAR

THOMAS S SAUNDERS, M D

AND

WILL C DAVIS, M D

PORTLAND, ORE

IN July 1939, Guy, Jacob and Weber <sup>1</sup> published a formula for a synthetic tar which was similar to crude coal tar but minus the inert substance (pitch) and the irritating (light) oils. They incorporated this synthetic tar in an ointment containing solution of aluminum acetate, wool fat and paste of zinc oxide with salicylic acid N F. They did not state the color of the finished product (probably white), nor did they give any account of its actual use in dermatologic practice.

Through the courtesy of the manufacturer <sup>2</sup> we were recently supplied with a synthetic coal tar cream (of pink color) for clinical trial in the treatment of diseases for which crude coal tar might ordinarily be used. The formula is as follows:

	Per Cent
Anthracene	0.066
Naphthalene	0.654
Phenanthrene	0.240
Carbazole	0.138
Picoline	0.033
Quinoline	0.038
Phenol (U S P)	0.042
Cresol (U S P)	0.047
Water	50.0
Triethanolamine stearate	
Cetyl alcohol	
Glycerin	
Petrolatum	
Colored with amaranth and flavored with oil of jasmine	

1 Guy, W H, Jacob, F M, and Weber, F. Synthetic Tar Paste. A Therapeutic Suggestion, Arch Dermat & Syph **40** 90-91 (July) 1939

2 Medical Research Division, Sharp & Dohme, Inc, Glenolden, Pa

The preparation was prescribed in 38 cases, in which seventeen different dermatologic entities were represented as follows

	Number of Cases
Eczema, hands	2
Eczema, atopic	4
Eczema, legs	1
Eczema, unclassified	1
Eczema, fingers	4
Eczema, infantile	2
Eczema, infectious	1
Eczema, asteatotic	1
Eczema, nummular	1
Eczema, ear canals	1
Dermatophytosis	1
Contact dermatitis	5
Dermatophytid	1
Neurodermatitis	4
Allergic dermatitis (patient sensitive to wheat)	1
Pompholyx	1
Pruritus ani	1
Indeterminate type (contact dermatitis vs neurodermatitis)	1
No reports available	5

### RESULTS

In 17 cases in which the involvement was bilateral, the eruption on one side was treated with a control ointment (3 per cent sulfonated bitumen in paste of zinc oxide N F, crude coal tar ointment, or a proprietary tar ointment) In every instance the synthetic tar cream was quite as effective as the control ointment The reverse was also generally true, i e, if the control applications were of no benefit, the synthetic tar cream was likewise ineffective In 16 other cases the synthetic tar worked about as well as remedies which would otherwise have been prescribed No reports were available in 5 cases In order to obtain as accurate a picture as possible, roentgen ray treatments and/or additional therapeutic measures were not used while the synthetic tar cream was employed An exception to this general rule occurred when control areas were being treated with another ointment

A recapitulation of the results follows In 4 cases the eruptions (chronic eczema, allergic dermatitis, infectious eczematoid dermatitis

and contact dermatitis) improved considerably with the synthetic tar ointment. In 5 cases there was moderate improvement of the eruptions (contact dermatitis, dermatophytosis, chronic eczema [2 cases], and dermatophytid). In 11 cases the eruptions (neurodermatitis [2 cases], atopic dermatitis [2 cases], asteatosis, contact dermatitis [2 cases], nummular eczema, contact dermatitis versus neurodermatitis, eczema of the ear canals and pompholyx) were slightly improved. In 11 cases there was no improvement of the eruptions (infantile eczema [2 cases], neurodermatitis [2 cases], atopic eczema, chronic eczema of the hands [2 cases], eczema of the fingers [3 cases] and pruritus ani). In 2 cases the eruptions (contact dermatitis and atopic eczema) were irritated.

#### SUMMARY

Clinical experiences with a synthetic coal tar ointment are described. The preparation as compared with ointment of coal tar N F, appears to be equally effective, with the additional advantage of pharmaceutical elegance and cleanliness. Judging from the results obtained in our cases, one cannot predict which dermatosis will respond and which will not, since in comparable cases the treated skins failed to react in the same manner or degree. This uncertainty of action applies to practically all local measures, however, and we do not feel that it detracts from the recognition of the synthetic tar cream as a useful therapeutic agent.

Medical Arts Building  
Medical-Dental Building

## ACUTE SYPHILITIC BILATERAL TOTAL OPHTHALMOPLÉGIA

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HUNTINGTON, W VA

THE FOLLOWING unusual case of acute syphilitic bilateral total ophthalmoplegia was observed in the Eye Clinic of Hospital 97 and is recorded because of the associated diagnostic and therapeutic problems which were presented

### REPORT OF A CASE

The patient was unable to see his way into the clinic, had to grope and was aided to the examination chair. An external examination of the eyes revealed a suggestive exophthalmos and no enophthalmos, but there was pronounced ptosis bilaterally. The patient could not elevate the upper lids to any extent, and only small palpebral apertures, approximately 2 to 3 mm, were visible. The borders of the lids showed no abnormalities, and the lashes showed a normal configuration. By manual manipulation, the palpebral and bulbar conjunctivas were brought into view, and no abnormalities were noted there. The caruncles and lacrimal apparatus appeared normal. By manual elevation of the upper lids, it was noted that the eyes showed decided external inferior rotation bilaterally. There was loss of motility, except for some small deviation, approximately 5 degrees, toward the internal canthus bilaterally. The patient stated that when the lids were elevated by manipulation he saw a confusion of images, and it made him dizzy. The corneas were clear, and there were no abnormal findings. The anterior chambers were well formed and filled, and the irises showed the same brownish pigmentation, with the pupillary aperture decidedly dilated and with no reaction elicited to light or in accommodation. With manual elevation of the upper lids, the fundi were examined minutely. The media were clear, and the disks were entirely normal, with mild physiologic cupping. The vessels showed no unusual features, and there appeared to be the normal arteriovenous relationship. The ocular muscles were examined individually, and it was noted that on both sides there was complete external ocular motor paralysis with only the contracted action of the lateral rectus and the superior oblique present. With loss of reaction both to light and in accommodation, there was also present complete internal ophthalmoplegia, or acute bilateral total ophthalmoplegia. With the upper lid elevated manually and the head rotated in a direction opposite to the lateral deviation of the eye being examined, the patient showed a manifest vision of 20/30 in the right eye and 20/30 — 2 in the left eye. The fact that he could see no Jaeger test type at any distance indicated paralysis of accommodation.

A brief neurologic examination showed that the patient swayed somewhat in a Romberg position. Deep reflexes were present and equal but moderately

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From the Department of Ophthalmology, Ohio State University College of Medicine, Columbus, Ohio

increased. Superficial reflexes were present but sluggish. There appeared to be an involvement solely of the third cranial nerve, the other cranial nerves appeared to be intact. There was a positive Babinski sign on the left side, and unsustained ankle clonus was noted on the same side. There was also a speech defect. In view of these findings, serologic examinations of the blood and the spinal fluid were requested and potassium iodide medication was prescribed. The patient was given 15 drops of solution of potassium iodide three times a day.

Two weeks later, on June 4, the patient was again examined, with the findings the same as before except that the right pupil appeared larger than the left and showed a mild reaction to light. The blood gave negative Wassermann and Kahn reactions, which helped to confuse the picture. However, the treatment was continued, and on June 6 the laboratory reported the following results of the examination of the spinal fluid: positive reaction for globulin, 15 cells, a Wassermann reaction of 3 plus in 0.5 cc of spinal fluid, 2 plus in 0.4 cc, 1 plus in 0.2 cc and 1 plus in 0.1 cc. The Lange colloidal gold test showed 555553321 configuration and the Takata-Ara reaction was 3 plus. In view of these findings, the dose of potassium iodide solution was increased to 20 drops three times a day, and a subsequent course of bismuth subsalicylate as initial intramuscular antisyphilitic therapy was prescribed.

When he was admitted to the hospital, the patient could not get around the ward because of the extreme ptosis and the lateral deviation of both eyes, which necessitated his groping along the walls and asking aid of the other patients to attend to his needs. Approximately two weeks after therapy with potassium iodide was begun, the right pupil began to show some reaction to light, rather sluggish but definite. Approximately three weeks after the beginning of this treatment, the patient's ptosis was not so great in either eye, and he began to have troublesome symptoms of diplopia. Approximately one month later, on June 20, the ptosis was less, and the lower half of the pupillary area was visible in each eye. There was some mild improvement in ocular motility bilaterally. However, the general position of the eyes remained as noted previously. Approximately six weeks later, the external ocular motor paralysis on the left side had cleared almost completely. The eyeball had moved into a more medial position, and there were some movements on attempting to follow various articles in the line of vision. The pupils now, however, were unequal, the right being larger than the left. The patient was started on bismuth subsalicylate therapy, and he could now get around the ward without much aid. Therapy with potassium iodide was continued for one more week and then discontinued. On July 21 the patient was reexamined. He no longer had any signs of ptosis of either eye, and the external ocular ophthalmoplegia had cleared completely, so that he was able to move his eyes in various directions, exercising all the muscles innervated by the oculomotor nerve. There was sluggish reaction to light bilaterally, and reaction in accommodation was present. He has been seen at subsequent intervals since that time, and the external and the internal ophthalmoplegia have cleared completely with active antisyphilitic therapy, consisting of alternate series of bismuth subsalicylate and tryparsamide.

#### COMMENT

The first considerations in this case were of course the location and the type of lesion present. With involvement of all the ocular muscles innervated by the third nerve and iridoplegia, the lesion was one which involved the function of all the oculomotor nerves bilaterally. By

elimination, the site where both oculomotor nerves could be involved readily with involvement of the iridoconstrictor nucleus (Edinger-Westphal nucleus) was at the site of the lower motor neuron or nucleus of the oculomotor nerves in the midbrain. Briefly, these neurons or nuclei of the oculomotor nerve lie alongside one another in the gray matter below the aqueduct of Sylvius in the midbrain, extending for 6 to 7 mm between the areas of the third and fourth ventricles. In caricature, the nuclei are reminiscent of an anterior view of a rabbit's head, with a row of cells strung parallel to this head on each side. A line drawn vertically down the center of this caricature would separate the nuclei into the right and left components of the oculomotor nucleus. The ears represent the Edinger-Westphal nuclei, one on each side, while the face represents Perlia's nucleus. On each side, the five cells represent the nuclei of the extraocular muscles, namely, the levator palpebrae superioris, the medial rectus, the inferior oblique and the inferior rectus, in the order named, from superior to inferior. A lesion covering the small area of these nuclei would blot out the entire lower motor neuron or nucleus of the third nerve and the Edinger-Westphal nucleus, producing a true total, bilateral, external and internal ophthalmoplegia. This, then, was taken as the location of the lesion in this case. Peters<sup>1</sup> stated that even a small pathologic area in the aqueduct of Sylvius or floor of the fourth ventricle is likely to involve the nuclei bilaterally, and Boyd<sup>2</sup> noted that frequently in syphilis of the central nervous system the floor of the fourth ventricle is involved in an inflammatory type of lesion, consisting of a dense perivascular collection of lymphocytes and plasma cells. There are also neuroglial proliferations, especially in the walls and the floor of the ventricles. "In the floor of the fourth ventricle, the glial proliferation causes an irregular heaping up of the floor."

The differential diagnosis of this lesion prior to laboratory examinations presented some confusion. The factors producing such a lesion rested between hemorrhage, tumor, trauma, syphilis, encephalitis and various other diseases of the central nervous system. However, in this case the onset was acute, and prior to the patient's admission to this hospital it was the impression that he had sustained a cerebral hemorrhage. The neurologic examination undertaken at the Eye Clinic disclosed that there was an involvement of only the third cranial nerve. This tended to localize the lesion, with further notation that there are no other cranial nerves in the immediate vicinity of the third nerve, excepting the fourth nerve, which occupies a position somewhat inferior and removed from the lower motor neuron or nucleus of the oculomotor

1 Peters, L. C. *The Extra Ocular Muscles*, Philadelphia, Lea & Febiger, 1941.

2 Boyd, W. *Textbook of Pathology*, ed 2, Philadelphia, Lea & Febiger, 1934, pp 909-910.

nerve The deep reflexes were exaggerated, the superficial reflexes were sluggish, a positive Babinski sign was noted, and the speech defect suggested a syphilitic type of involvement The negative Wassermann and Kahn reactions of the blood added an element of confusion, but a subsequent examination of the spinal fluid revealed the full-blown dementia paralytic type of syphilitic involvement Peters,<sup>1</sup> Duke-Elder,<sup>3</sup> Gifford, Fuchs<sup>4</sup> and May<sup>5</sup> have written that the acute bilateral type lesion due to syphilis and with complete recovery is unusual and is seen infrequently Fuchs further stated that the syphilitic involvement of the cranial nerve is most commonly of the chronic type, producing gradual degeneration and atrophy of the gray substance, with irreparable damage, and is as a rule incurable It has been claimed, moreover, that internal ophthalmoplegia is frequently a sign of cerebral syphilis Fuchs<sup>4</sup> said

*Acute ophthalmoplegia* develops within a few days and is combined not infrequently with drowsiness It is observed after poisoning (by alcohol or lead, botulismus, carbon monoxide gas) and after acute infectious diseases (diphtheria, influenza, measles, etc), in which case also it is probably a toxic affect that is in question It occurs, moreover, under the form of a disease analogous to the poliomyelitis of children In all these cases there is an acute inflammation in the region of the nuclei Such cases may go on to recovery, but may also end in death by transfer of the process to the deeper motor nuclei of the medulla oblongata with subsequent respiratory paralysis

Andre<sup>6</sup> described a case of bilateral ophthalmoplegia due to intracranial propagation of a cancer of the right maxillary sinus, while Ayres<sup>7</sup> described a case of unilateral total syphilitic ophthalmoplegia, which seemed to confirm what has been quoted in the preceding paragraph

The acute symptoms in the case reported here were rather complete and conclusive, as was the recovery It is interesting to note that the diplopia in this case was most distressing and to the point of nausea, indicating that simultaneous macular perception was not destroyed by the lesion Syphilis of the central nervous system was the cause, and the treatment as noted in the report of the case was instituted along these lines On confirmation of this impression by laboratory findings the dosage of potassium iodide was increased, and antisymphilitic therapy was

3 Duke-Elder, W S Textbook of Ophthalmology, St Louis, C V Mosby Company, 1943

4 Fuchs, E Text-Book of Ophthalmology, edited by A Duane, ed 5, Philadelphia, J B Lippincott Company, 1917

5 May, C H Diseases of the Eye, Baltimore, William Wood & Company, 1941

6 Andre, M Bilateral Ophthalmoplegia Due to Intracranial Propagation of a Cancer of the Right Maxillary Sinus, J belge de neurol et de psychiat 40.21-27 (Jan) 1940

7 Ayres, F Total Syphilitic Ophthalmoplegia, Brasil-med 56 405-406 (Aug 22-29) 1942

instituted The patient made an uneventful recovery after eight weeks of treatment and at the present time shows no residuals of the total bilateral ophthalmoplegia

#### CONCLUSIONS

Acute syphilitic bilateral total ophthalmoplegia, although seen infrequently, appears to respond readily to antisyphilitic therapy, in direct contrast to chronic syphilitic ophthalmoplegia, which is frequently incurable

The patient in this case had negative serologic reactions of the blood, but a subsequent examination of the spinal fluid revealed the full-blown dementia paralytica type of syphilitic involvement

The diplopia noted in this case was extremely distressing because of the fact that simultaneous macular perception was not involved at any time

# Clinical Notes

## PEMPHIGUS FOLIACEUS

A Patient Treated with an Unusual Amount of Acetarsone

WILLIAM H GOECKERMAN, M D, LOS ANGELES

E W, a white woman 52 years of age, when first seen in September 1942 had a vesicobullous eruption involving almost the entire body, including the mouth, vagina and rectum. She had lost 25 pounds (11.3 Kg) in weight and was confined to her bed. The eruption had been of a year's standing and had received a variety of haphazard treatment. In the early phase of the eruption a dermatologist had made a diagnosis of erythema multiforme, but treatment for this had not been systematic. When seen by me it was a typical case of advanced pemphigus vulgaris, with possibly a tendency to the foliaceus type. In September 1942 she was given acetarsone, 0.25 Gm, according to the regimen advocated by Oppenheim. Response was prompt. In order to try the effect of suramin sodium, the administration of acetarsone was interrupted. Suramin sodium was, however, poorly tolerated, so in December 1942 she was again given acetarsone. Since the skin and general health again promptly improved, she was given synthetic oleovitamin D, thiamine hydrochloride and asiatic pills (a preparation containing arsenic trioxide) in the hope that milder measures might hold the improvement. She promptly relapsed, however, in about a month, and again was given acetarsone with calcium regularly. This was continued without interruption for about six months, despite prompt improvement. At this time, after discontinuance of the use of acetarsone for about a month, there appeared a profuse eruption on the skin which was entirely different from her original eruption and in no way suggested pemphigus. It was pruritic and consisted of large erythematous plaques chiefly on the trunk. In some areas of this erythema there were grouped papulovesicles, the picture suggesting dermatitis herpetiformis. It was at first thought that it might be a toxic eruption from the acetarsone, because by this time the patient had taken a considerable amount of the drug. Various measures were tried to relieve the patient of her discomfort, but since nothing helped, she was again given acetarsone. Again improvement was prompt. Use of the drug was then continued fairly regularly for nearly a year, to the fall of 1944, when again an eruption resembling dermatitis herpetiformis appeared. It was then decided to try administration of sulfapyridine for the eruption, but there was no benefit, so she was again given acetarsone, with benefit. This was continued in a fairly systematic manner, the scheme outlined by Oppenheim always being adhered to closely until July 1945, when there was complete absence of any eruption. The patient then remained free from cutaneous manifestations for more than six months without any drugs. In February 1946 she was again seen with the peculiar eruption resembling dermatitis herpetiformis. She was given acetarsone in the usual manner, with the usual response, and she has now taken over 900 tablets of 0.25 Gm each, without showing the slightest inconvenience from the drug.

So far as I was able to learn, this patient took the largest amount of acetarsone ever given. It illustrates the enormous difference in tolerance to drugs by

different persons. An interesting feature also was the cutaneous relapse to an eruption entirely different from the original picture, resembling somewhat dermatitis herpetiformis. While this eruption was puzzling when it occurred, in retrospect, having observed the patient for nearly four years, I cannot escape the feeling that acetarsone in this patient changed what is ordinarily a vicious systemic disease to an essentially cutaneous one. Being fully aware of the diagnostic difficulties involved in pemphigus, there need be no quibbling about the original diagnosis, for if it is ever possible to make a diagnosis of pemphigus on clinical grounds this was a case of the advanced condition when first seen.

1216 Roosevelt Building

## PIGMENTATION FOLLOWING APPLICATION OF IRON SALTS

Report of a Case in Which It Was Not Permanent

MAURICE J. STRAUSS, M.D., NEW HAVEN, CONN.

Until fairly recently, iron salts (ferrous sulfate or ferric chloride) have been widely used in the treatment of dermatitis caused by contact with the poison ivy plant. In 1917 Pusey<sup>1</sup> called attention to the possibility of permanent pigmentation as a result of the use of iron salts. In the case reported by him the iron salt used was ferrous sulfate, 1 ounce (30 Gm.) to 1 gallon (4,000 cc.) of vinegar. Despite Pusey's warning this form of treatment remained popular and even gained in popularity, possibly because of the work of McNair<sup>2</sup> in 1921. In 1936 Traub and Tennen<sup>3</sup> reported 2 cases observed by them in which a permanent pigmentation occurred following the use of ferric chloride solution in the treatment of dermatitis venenata. They also mentioned 4 cases which had come under the observation of McKee some years before. Then in 1937 Sutton<sup>4</sup> reported a further case. All these writers used the word permanent, and it has since been a generally accepted fact that the use of iron salts in the treatment of dermatitis venenata should be discouraged.

While I am not advocating the use of iron salts in the treatment of this condition, the following brief report of a case is evidence that this form of pigmentation is not necessarily permanent.

### REPORT OF A CASE

A 21 year old white woman was first seen in June 1939. She was known to be sensitive to the poison ivy plant and had previously been treated for an eruption typical of that caused by this plant. When seen in June 1939, she had been away at a New England college. She had suffered a severe attack of dermatitis venenata and had been treated with a solution of ferric chloride. She presented on the posterior surface of each leg an irregularly shaped area of brownish pigmentation. These areas were sharply demarcated, and the overlying skin was

1 Pusey, W. A. Brown Stains in the Skin from Wet Dressings of a Solution of Copperas, *J. A. M. A.* **68** 627 (Feb 24) 1917.

2 McNair, J. B. A Contribution to the Chemotherapy of Rhus Dermatitis and Tentative Method for Treatment, *Arch. Dermat. & Syph.* **3** 802 (June) 1921.

3 Traub, E. F., and Tennen, J. S. Permanent Pigmentation Following Application of Iron Salts, *J. A. M. A.* **106** 1711 (May 16) 1936.

4 Sutton, F. L., Jr. Pigmentation of the Skin Due to Iron (Copperas) Applied Locally, *J. A. M. A.* **108** 112 (Jan 9) 1937.

smooth The patient was told that this pigmentation was permanent and that nothing could be done about it It did not seem important to have a photographic record made This is regrettable because when she was next seen, in August 1945, over six years later, she stated that the pigment had been gradually disappearing until it had reached its present condition On examination there were found only a few pinhead-sized to lentil-sized areas of pigmentation where the large brown areas had been

#### COMMENT

Although the writers who have previously reported cases of pigmentation from iron salts all spoke of it as a permanent pigmentation, Pusey did so with some reservation In describing the condition, he stated that the patient reported to him two years after he saw her that the spots were growing lighter Also, he stated in the closing paragraph of his report, "I am told that particles of iron in the eye usually in time completely disappear These particles are too large to be removed by phagocytes, and if they disappear it must be by their gradual solution This suggests the possibility of the ultimate disappearance of iron stains in the skin, but the course of this case thus far indicates that this disappearance, if it takes place, will be only after a very long time"

In Pusey's patient the spots were reported to be lighter after two years, while in the case reported here large areas of pigmentation have gradually disappeared After a period of six years there is only enough pigmentation left to be just discernible

#### SUMMARY

A case is reported in which pigmentation resulting from the use of ferric chloride in the treatment of dermatitis venenata caused by the poison ivy plant has almost entirely disappeared over a period of six years

41 Trumbull Street.

## Obituaries

### ERNEST DWIGHT CHIPMAN, M D

1875-1946

Dr Ernest Dwight Chipman was born in New Haven, Conn , on March 6, 1875 and died on Dec 4, 1946 His premedical education was obtained at Phillips Academy at Andover, and at Yale University School of Medicine he received the degree of M D

Dr Chipman practiced for a few years in Waterbury, Conn , and from 1905 for the rest of his life in San Francisco In his early days he was instructor in dermatology in Cooper Medical College and was dermatologist at the San Francisco Polyclinic Later, he served as dermatologist to the German Hospital and Mary's Help Hospital and was consulting dermatologist to Mount Zion Hospital

He was a member of the Connecticut State Society from 1898 to 1905 After that he was a member of the California State Medical Society and a fellow of the American Medical Association He was a member of the San Francisco Academy of Medicine and the California Pediatric Society He was elected a member of the American Dermatological Association in 1914 and was a corresponding member of the French Dermatological Society

Dr Chipman served as a medical officer in World War I, being attached at first to Base Hospital 67 Later he became a consultant to the 30th Division, and still later to the 2d Corps, United States Army, serving with the 4th British Army

The social clubs to which he belonged included the Bohemian, S F , the Marin Golf and Country Club and the Meadow Club of Tamalpais His favorite amusements were golf, tennis and duck shooting

Dr Chipman married Miss Jane Beaman Greenwood in Belvedere, Calif , on Oct 3, 1900 They had no children

The following tribute was written by Dr Langley Porter, a close friend of Dr Chipman "Ernest Chipman was ever a loyal colleague, respected and admired by his fellows Equally, he was a friend to his patients, whose personal, social and economic difficulties were always important to him, for he was one who realized that the physician, no matter how specialized, needs to know a sick person's total life situation if he is to accomplish the utmost in healing

"Dr Chipman's arduous long last illness deprived his colleagues of his companionship for all too many years But every one who knew the handsome, genial man who was Ernest Chipman will remember him with affection and will be moved to the deepest regret that he is gone"



ERNEST DWIGHT CHIPMAN, M.D.  
1875-1946

## News and Comment

### DR FOX RESIGNS AS CHIEF EDITOR

Dr Howard Fox resigned as Chief Editor of the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY on March 1, 1947

Dr Fox became editor of the ARCHIVES in 1937, on the retirement of Dr William Allen Pusey, who had been editor since the periodical was taken over by the American Medical Association in 1920. He has maintained the ARCHIVES as the world's foremost dermatologic publication under the trying conditions imposed by World War II. In a subsequent issue recognition of his efforts will be given.

## Abstracts from Current Literature

THE INVASIVE CHARACTER OF CANCER GROWTH DALE REX COMAN, Am J M Sc  
211 257 (March) 1946

Coman discusses invasiveness—that feature of malignant tumors which allows them to disrupt the surrounding tissue, dislocating the normal cells and often destroying them. He points out that it is not the pressure of a capsule which keeps benign tumors localized, malignant tumors do not differ from benign ones by peripheral versus central growth, increased pressure within the tumor or the production of destructive ferments. The most evident difference appears to be the relative lack of cohesiveness of cancer cells, demonstrated by a technic which measures the force required to pull apart a pair of cells. Malignant cells, whether from the lip or cervix, consistently showed low values of cohesiveness as compared with normal and benign tumor cells.

The author theorizes on the cause of cohesiveness of cells, regarding it as dependent on the state of the cement substance that is known to exist between cells, which serves to bind them together. Perhaps the explanation lies in local deficiency of calcium, a hypothesis which finds support in the chemical analysis of cancer tissue. Or the defect may relate with abnormality of the "spreading factors" which enhance the spread or diffusion of small particles or solutions through living tissues. Experiments of others suggest that lack of cohesiveness of cancer cells may depend on the excessive presence of a potent spreading factor, an enzyme called hyaluronidase, which can be extracted from testicular tissue.

EFFECT OF SODIUM BICARBONATE ON THE THERAPEUTIC EFFECTIVENESS OF SULFADIAZINE IN MICE ARTHUR KORNBERG, Am J M Sc 211 286 (March) 1946

Sodium bicarbonate in large amounts greatly depressed the blood concentrations and the therapeutic effectiveness of sulfadiazine in mice inoculated with pneumococci. These effects could be overcome by raising the dosage of sulfadiazine. Kornberg suggests that when sodium bicarbonate is used to prevent renal lesions close attention should be given to the maintenance of therapeutically effective blood levels of sulfadiazine.

LYNCH, St Paul

VENEREAL DISEASE IN THE ARMY AIR FORCES IN THE CONTINENTAL UNITED STATES, 1942-1944 ROBERT DYAR and J R SCHOLTZ, Am J Syph, Gonorr & Ven Dis 30 99 (March) 1946

The authors discuss the program for control of venereal disease of the Army Air Force during the period of 1942 to 1944. From 1942 to 1944 the time lost from duty per case of venereal disease dropped from fifteen to four days as a result of better medical administration, improved methods of treatment and the introduction of penicillin. At the end of 1944, less than 1 man in every 10,000 white soldiers and 1 in every 830 Negroes with the Army Air Force was off duty on any one day because of venereal disease.

THE USE OF PENICILLIN IN THE TREATMENT OF SYPHILIS OF THE CENTRAL NERVOUS SYSTEM B H KUHN, K A RILEY, J LAMAR CALLAWAY, RAY O NOOJIN and ARTHUR H FLOWER JR, Am J Syph, Gonorr & Ven Dis 30 110 (March) 1946

A preliminary report is made of 100 patients with active syphilis of the central nervous system, each treated with a total of 4,000,000 units of penicillin over a ten day period, 50,000 units of penicillin every three hours for a total of eighty injections. Sixty per cent of this series of patients have shown clinical improve-

ment associated with definite improvement in the findings on examination of the spinal fluid, 31 per cent clinical improvement alone, 4 per cent improvement in the findings on examination of the spinal fluid unassociated with clinical change and 5 per cent decided clinical deterioration with no improvement or progression in the findings on examination of the spinal fluid. In 8 per cent of the total negative Wassermann reactions of the spinal fluid have developed.

The patients with no previous therapy have apparently responded best to penicillin, while those with previous adequate chemotherapy have shown the poorest response. Febrile Herxheimer reactions have been frequent, but there have been no reactions necessitating the termination of therapy.

The authors are of the opinion that results with penicillin therapy will for the moment, in the limited period of observation, bear comparison with those of fever therapy. Its effect has been equal to or superior to that obtained by longer, more expensive more reactive fever therapy, arsenotherapy or treatment with heavy metals.

**PENICILLIN THERAPY OF EARLY SYPHILIS IN 14,000 PATIENTS FOLLOW-UP EXAMINATION OF 792 PATIENTS SIX OR MORE MONTHS AFTER TREATMENT**  
DONALD M. PILLSBURY, Am J Syph, Gonorr & Ven Dis **30** 134 (March) 1946

Over 14,000 patients with early or latent syphilis or with syphilis which had not responded satisfactorily to previous treatment with standard or intensive arsenobismuth therapy received treatment with penicillin.

The system of treatment employed in all patients consisted of a total of 2,400,000 Oxford units of sodium penicillin, divided into sixty intramuscular injections of 40,000 units each at three hour intervals for a total period of seven and one-half days.

Infectiousness, with rare exceptions, was controlled promptly. The incidence of infectious relapse after penicillin was low and will usually occur within twenty weeks after treatment.

Achievement of seronegativity six months after the initial treatment is significantly lower in seropositive primary and in secondary syphilis than in seronegative primary syphilis. The incidence of asymptomatic neurosyphilis disclosed by examination of the spinal fluid performed six to eight months after treatment is extremely low. The initial promise of penicillin as the best single agent against syphilis is being fulfilled.

**THE PROBLEM OF REINOCULATION OF HUMAN BEINGS WITH SPIROCHETA PALLIDA**  
HERMAN BEERMAN, Am J Syph, Gonorr & Ven Dis **30** 173 (March) 1946

The author presents an exhaustive review of the literature dealing with reinoculation of human beings with *Treponema pallidum*.

Reinoculation with *T. pallidum* is successful in all phases of untreated human syphilis (superinfection), but in dementia paralytica the number of successful reinoculations is small. The reinoculation lesions have a tendency to resemble those representing the phase of syphilis that the patient is in at the time of reinoculation.

Reinoculation of patients supposedly "cured" of syphilis (reinfection) has rarely been reported. The data on reinoculation of human beings with syphilis are not of sufficient size to answer definitely the question as to whether reinfection is possible in human beings. While there is evidence that reinfection (or superinfection) may occur, the data cannot be construed as a rational basis for the now numerous cases of reinfection reported in patients treated by intensive therapy for syphilis (this is especially applicable for the number of cases of reinfection reported following penicillin therapy).

However, since there are no absolute criteria of biologic cure or adequate means to identify asymptomatic infections in human beings, it is possible that reinfections may take place on a scale larger than hitherto suspected.

REUTER, Milwaukee

THE ROLE OF VITAMINS IN THE PATHOGENESIS AND TREATMENT OF SKIN DISEASES.  
L N MASHKIELEISON, E B BENYAMOVICH, E D KRICHEVSKAYA and L V  
SHATAMOVA, *Am Rev Soviet Med* 3.19 (Oct) 1945

The metabolism of ascorbic acid and its therapeutic effect were studied in cases of erythroderma, psoriasis, eczema, pyogenic infections and pityriasis rubra. Patients received daily doses of 300 mg of ascorbic acid intravenously or 600 mg orally. Fifty per cent of the patients with erythroderma showed improvement. Gratifying to excellent results were obtained in some cases of eczema, psoriasis, neurodermatitis and furunculosis. In only 11 out of 85 cases were the results from use of ascorbic acid completely unsuccessful. The authors feel that ascorbic acid should be used freely in the treatment of cutaneous diseases as an adjunctive method.

The blood of patients with eczema, ichthyosis, keratosis, follicular hyperkeratosis, keratosis follicularis and pityriasis rubra were examined for blood carotene levels and vitamin A values. The blood carotene levels were found to be normal, but the vitamin A values were below normal in cases of ichthyosis, follicular hyperkeratosis, keratoderma of palms and soles and keratosis follicularis. This would seem to indicate that the transformation of provitamin A in these diseases is impaired and insufficient intake of fats and diminished function of the gastrointestinal or biliary tract and, particularly, of the reticuloendothelial system may be responsible. The authors attach a great deal of significance to this fact. They think that it explains why in some cases of frank "A" hypovitaminosis massive doses of carotene fail to cause any improvement. As a result of these findings, concentrated vitamin A in doses of 100,000 units was administered daily. An increase in the blood level of vitamin A followed and was accompanied with improvement in the condition of the skin of the patients. Best results were obtained in follicular keratosis, pityriasis rubra and seborrheic dermatitis.

Riboflavin was used to treat various dermatoses. It was administered in 5 mg doses two or three times daily for one to four weeks. Relief of itching in seborrheic dermatitis was noted after several days of treatment. Gratifying results were obtained in rosacea, but the drug had to be supplemented with nicotinic acid before the rosacea completely cleared. Complete cure was obtained in 5 cases of cheilitis and 2 cases of black tongue. Riboflavin was useless in lichen planus.

Nicotinic acid alone was used in 62 cases of various dermatoses. Most patients received 0.1 Gm of nicotinic acid three to five times a day for two to three weeks. The greatest therapeutic result was to ameliorate or stop completely the pruritus occurring in lichen planus and eczema. The objective symptoms disappeared in 30 patients suffering from rosacea, seborrhea, neurodermatitis and parapsoriasis. Fifteen patients did not show any improvement at all, while 17 patients were slightly to moderately improved.

The authors feel that the vitamins are an excellent adjunct to treatment and that cutaneous diseases which do respond to vitamin therapy need not be regarded as avitaminoses. Apart from their pure action as vitamins, the vitamins exert a pharmacodynamic curative effect and a regulating influence on numerous processes in the organism.

PENICILLIN IN PREVENTION OF PRENATAL SYPHILIS. MARY STEWART GOODWIN  
and JOSEPH EARLE MOORE, *J A M A* 130 688 (March 16) 1946

Thirty-one mothers, all of whom had early infectious syphilis, were treated with penicillin. All these syphilitic pregnant women were delivered of normal infants. Pregnancy did not exert any effect in slowing up serologic response, since the pregnant patients reverted toward seronegative at the same rate as non-pregnant patients. Abortion is not more frequent during penicillin treatment of the mother than during other forms of antisyphilitic treatment. It is recommended that in syphilitic pregnant women penicillin be used routinely for the prevention of prenatal syphilis. The total dose of penicillin should not be less than 2,400,000 units over a period of seven and one-half days.

DESENSITIZATION TO INSECT BITES ALEXANDER HATOFF, J A M A **130** 850  
(March 30) 1946

One hundred and twenty-nine susceptible infants and children were immunized against flea bites. The flea antigen used consisted of an extract of the whole fleas of cats, dogs and human beings (*Ctenocephalides felis*, *Ctenocephalides canis* and *Pulex irritans*). The average number of injections of flea antigen given was four. One hundred, or 78 per cent, of the patients were benefited.

HENSCHER, Denver

SOME OBSCURE AND PARADOXICAL PROBLEMS OF SYPHILIS UDO J WILE, Proc  
Inst Med Chicago **16** 246 (Nov 15) 1946

The obscure and paradoxical character of syphilis observed clinically, in the laboratory and in animal experiments, is noted first in the infecting organism itself which, in spite of twenty-five years of research, still cannot be distinguished morphologically from the organisms causing yaws and pinta and from the non-pathogenic *Spirochaeta microdentium*.

Laboratory experiments show that no domesticated animal can be infected with syphilis in precisely the same manner as the human host. Even in the anthropoid apes the disease differs in its modification and in the spontaneous resolution of its course. Various strains of white and gray mice as well as the Egyptian hamsters can readily be inoculated with various strains of rabbit-born human syphilis. Animals so inoculated are capable of infecting rabbits by the introduction of brain, spleen, gonads and lymph node substance, however, in no instance do the infective inoculums show either pathologic evidence of the disease or any organisms by dark field examination. The syphilis-bearing mice are invariably seronegative in reaction although the infected rabbits always show a seropositive blood reaction. Furthermore, the syphilis-infected mice are unable to convey this infectiousness to their offspring.

It is thought that the mice carry the syphilis organism in an infravisible or possibly granular form, which may explain the reactivation of latency and the transmissibility of occult syphilis in conjugal infections. This form may also be the activating factor in interstitial keratitis.

In acquired human syphilis there is a peculiar affinity for the endothelial lining and musculature of blood vessels, bony structure and the parenchyma of the brain, liver and testes and a peculiar avoidance of the parenchyma of the thyroid, pancreas, kidney and ovary. There is also an unexplainable paradoxical affinity during the early and late manifestations of the disease for structures lined with squamous epithelium, whereas structures lined with columnar epithelium are rarely if ever involved.

The reproductive organs of both sexes present a curious paradox in that the testes are frequently involved in the acquired infection while syphilis of the ovaries does not exist. Another peculiarity is that, while most infections during gravidity are viewed with alarm, syphilis in the pregnant woman runs a milder course. Whereas gross and microscopic changes in the smooth muscle of the heart and the blood vessels form an essential part of the pathologic changes in syphilis the smooth muscle of the uterine body is never involved.

Syphilis of the central nervous system presents the paradoxical involvement of the gray matter accompanied by a rich implantation of organisms in dementia paralytica and involvement of the white matter unaccompanied by demonstrable organisms in tabes. Also, by contrast, when other micro-organisms invade the nervous system serious clinical symptoms become manifest, whereas involvement by *Treponema pallidum* often produces no clinical symptoms.

In spite of the extensive involvements of the cardiovascular system acquired syphilis plays an inconspicuous role in either premature or senile arteriosclerosis. It is further paradoxical that in spite of pronounced changes at the base of the aorta, frequently extending to the aortic valves, major coronary occlusion is a clinical rarity.

Congenital syphilitic infections also present inconsistent and curious effects. Interstitial keratitis, one of the severe manifestations, is unique in the absence of

demonstrable organisms, resistance to treatment and involvement of the unaffected eye during energetic therapy. The tardy manifestations are likewise strange in that they frequently do not become manifest until accident, disease or pregnancy initiate their appearance. Likewise difficult to understand in congenital syphilis is the frequent finding of dementia paralytica and the extreme rarity of the tabetic syndrome as well as the absence of cardiovascular syphilitic disease.

Lastly, there is the peculiar behavior of the reagents in the blood stream. It is becoming increasingly clear as time goes on that the serodiagnostic procedures can be under many circumstances devoid of etiologic significance and lead to misinformation and needless therapeutic procedures.

The author points to the increasing list of diseases which give so-called false positive reactions and states that the time has arrived when much more critical appraisal must be made in the presence of a positive reaction than appeared necessary a decade ago.

RODIN, South Bend, Ind

FALSELY POSITIVE WASSERMANN AND KAHN REACTIONS IN INFECTIVE HEPATITIS  
J H WAELSCH, Brit M J 1 353 (March 9) 1946

A case of infective hepatitis with transient biologic false positive Wassermann and Kahn reactions is reported. The case was one of a large series met with while the authors were working on a routine scheme for investigation of jaundice and enlargement of the liver without jaundice.

SHAW, Chattanooga, Tenn

HERPES ZOSTER IN AN ISOLATED COMMUNITY E J S WOOLLEY, Brit M J 1 392 (March 16) 1946

On the island of Tristan da Cunha, in the South Atlantic, there lived some 220 persons, none of whom had ever suffered from chickenpox. In 1942 a party of military personnel was established on the island. In May 1943 the author saw there a typical case of herpes zoster. Such a disease had not been seen before by the islanders. The anticipated sequel, an epidemic of chickenpox, did not occur. No further cases of herpes zoster were seen until December 1943, when a typical outbreak developed in a man. Again no chickenpox followed. Three and a half months later, in March 1944, a third case of herpes zoster occurred. There were no further cases by the time the author left the island in July 1944, nor had there been any cases of chickenpox.

If there were conditions in which an epidemic of chickenpox might be expected to follow herpes zoster, they were present on this island, since none of the inhabitants had any acquired immunity to the virus and the people lived in crowded, dirty cottages. The author interprets the events as indicating that herpes zoster can be caused by neurotropic viruses other than the virus of chickenpox.

SHAW, Chattanooga, Tenn

OUT-PATIENT TREATMENT OF EARLY SYPHILIS WITH PENICILLIN T R LLOYD-JONES, S J ALLEN and E M DONALDSON, Brit M J 1 567 (April 13) 1946

On the hypothesis that a continuous level of penicillin in the blood stream is not necessary for the cure of syphilis, the authors adopted a scheme of intermittent penicillin therapy, with encouraging results. For primary syphilis they recommend eight daily, single injections of 500,000 units dissolved in 2 to 3 cc of sterile water and injected intramuscularly, giving a total dosage of 4,000,000 units. For secondary syphilis they recommend ten daily injections of 500,000 units each giving a total dosage of 5,000,000 units. Two series of patients were treated with single daily injections. Of 102 patients, 78 received 300,000 units intravenously for a total of 24 to 39 mega units, with a relapse rate of 9 per cent. The remaining 24 were given 500,000 units intravenously in a single dose daily for a total of 25 to 50 mega units, with a relapse rate of 42 per cent.

In the second series of 113 cases the patients were treated by the single daily intramuscular injection technic. One hundred and nine received 300,000 units in a single injection for a total of 24 to 45 mega units, with a relapse rate of 55 per

cent, while 4 patients received 500,000 units by a single, daily intramuscular injection for a total of 4 mega units, with a relapse rate of 0 per cent. The observation period in all patients ranged from three to ten months.

SHAW, Chattanooga, Tenn

A VISIT TO A LEPROUS COLONY P. P. NEWMAN, *Brit M J* **1** 616 (April 20) 1946

The author describes a visit to a leper colony in India which accommodated about 700 patients. The standard treatment was by injections of chaulmoogra oil in 4 per cent creosote or thymol. The results, on the whole, were good. As many as fifty injections were given with  $\frac{1}{4}$  inch (0.6 cm) needles into the skin around the leprosy areas in addition to daily intramuscular injections.

Syphilis and tuberculosis were common complications. Surgical amputations were frequently performed, despite which fact there was a remarkable degree of mobility and stability. Morale among the patients was surprisingly high, and it was obvious that the medical staff, despite working under inadequate conditions, was performing an excellent service.

SHAW, Chattanooga, Tenn

MODES OF TRANSMISSION OF HANSEN'S DISEASE (LEPROSY) B. MOISER, *Leprosy Rev* **16** 63 (Dec) 1945

The author states the belief that the name "Hansen's disease" should replace the term "leprosy" and that the word "leper" should be abolished. Hansen's disease is generally believed to be spread by long-continued, intimate contact. After sixteen years' work at a hospital in South Rhodesia, Moiser expresses the opinion that this view is entirely erroneous. He spent six years investigating the role which cockroaches play in the transmission of leprosy. Many hundreds were examined, and 69 per cent showed acid-fast "oval bodies" microscopically which had the appearance of Hansen's bacilli. Such bodies could not be found in ticks, bedbugs or flies. Similar bodies were found in the dried feces of cockroaches in such numbers as to suggest that they multiplied in the gut of the cockroach. Such droppings could be a source of infection and would explain why the disease is one affecting a house and family. The author states that further investigation is necessary to prove his theory.

PALM OIL IN LEPROSY L. LENGAUER, *Leprosy Rev* **16** 67 (Dec) 1945

The author tells of a native of South Nigeria in whom leprosy developed and who left his native village "from shame." He built himself a hut near some palm trees and accepted his fate. He began rubbing his skin with palm oil and drinking the uncooked oil. His health improved, and in a year he was cured. He tried the same treatment, with successful results, with others. The author used a palm oil ointment on chronic ulcers in leprosy and found it extremely satisfactory. He also administered 1 cup of palm oil daily by mouth. Most of the patients improved remarkably.

LAYMON, Minneapolis

INVESTIGATION INTO THE DEVELOPMENT OF TUBERCULOUS ALLERGY K. SIPOS, *Acta dermat-venereol* **22** 138 (March) 1941

A suspension of *Mycobacterium tuberculosis* in isotonic solution of sodium chloride was irradiated for fifty hours by quartz light and was used to inoculate guinea pigs intracutaneously, subcutaneously and intraperitoneally. All the animals thus sensitized responded with identical allergic phenomena regardless of the route of inoculation. When tested against tuberculin, a moderate hyperemia developed at the site of the test, which did not correspond to the type of reaction found in tuberculous animals. When tested with the bodies of the destroyed *Mycobacterium tuberculosis* the sites of the tests became inflamed and then suppurated. This differs in the type of reaction observed in tuberculous animals which are tested with the bodies of the dead organisms. There is in the tuberculous animals a necrosis at the site of the test rather than a suppurative process. Sipos concludes that the

reason for this difference is that tuberculous animals have a combined allergy to tuberculin and to the bodies of the organisms

RUBROPHEN IN CUTANEOUS TUBERCULOSIS T E OLIN, *Acta dermat-venereol* 22 150 (March) 1941

Rubrophen (a rosolic acid preparation) has an amazing curative effect on tuberculids and on ulcerated lupus processes. It has a beneficial effect on the tumidus type and no effect on the lupus planus variety. In respect to the latter two types of cutaneous tuberculosis, the drug is valuable only as an adjunctive method of treatment. At the onset there is a rapid regression of lesions. With continued treatment the improvement slows down, and after it has reached a certain stable point no further improvement can be expected. This phenomenon indicates the value of periodic rather than continuous treatment.

Contrary to the general opinion that the use of rubrophen will cause an increase in the number of red cells, a decrease may be observed. The drug evidently does not have any direct bactericidal effects. The results, rather, may be attributed to its power of stimulating and strengthening natural powers of resistance.

A CASE OF "PILI TORTI" R T BJORNSTAD, *Acta dermat-venereol* 22 242 (May) 1941

A woman 25 years old was presented with a peculiar anomaly of the hair, which she had since birth. The hairs were short, thin, easily broken and only loosely attached to the hair follicles. They were longitudinally furrowed and ridged and were twisted on their longitudinal axes as much as 180 degrees. Histologic examination of the scalp revealed slight superficial inflammation. Sebaceous glands were abundant. Immediately above the bulb the hair was round, but the ridges and furrows started deep in the follicular portion of the shaft. Similar changes were found in the eyebrows. Bjornstad was of the opinion that this was a congenital malformation, although no information as to its presence in other members of the patient's family was available.

SENSITIZATION TO EDIBLE MUSHROOMS S HELLERSTROM, *Acta dermat-venereol* 22 331 (Sept) 1941

An erythematous macular eruption accompanied with considerable edema was present on the hands and face of 2 women who had handled raw edible mushrooms for about twenty years without any cutaneous or general untoward reaction. For several years prior to this investigation both patients noted that cutaneous lesions developed after the handling of mushrooms.

A strongly positive reaction was obtained on 1 patient with patch tests of *Boletus luteus* L. and a weakly positive reaction to *Boletus edulis* Bull. The other patient demonstrated positive reactions to *Boletus luteus* L., *Lactarius deliciosus* and *Clavaria flava* Schaeff. In the latter case sensitivity to the allergenic mushrooms was also demonstrated on eating them fried. Boiling seemed to inactivate the allergenic properties of the fungi.

THE EFFECT OF TURPENTINE OIL ON NORMAL AND HYPERSENSITIVE SKIN I ROKSTAD and P BONNEVIE, *Acta dermat-venereol* 22 401 (Nov) 1941

The proportion of the hydroaromatic hydrocarbons (terpenes) which can be produced in the pure state by fractional distillation determines the properties of the various oils of turpentine in which they are contained.

These oils have both primary toxic and eczematogenous effects. At first it was believed that the latter effect was due to the impurities, but later it was realized that this was an inherent potentiality of the terpenes.

The purpose of this experiment was to determine these two properties of the various terpenes in oil of turpentine. Six substances—alpha-pinene, beta-pinene, delta (3)-carene, a mixture of monocyclic terpenes (of undefined composition), d + l limonene (dipentene) and the low boiling impurities in sulfate turpentine—were used in tests in concentrations of 0.1, 0.5, 1.5, 5, 15, 30, 45, 60, 75, 90 and 100 per cent.

The toxic effects of these substances were tested on persons known to be not sensitive to pinene, while the eczematogenous properties were tested on persons known to be strongly allergic to pinene. At first, ordinary patch test methods were used. It soon became evident that, for testing the toxicity of the terpin, the usual patch tests were useless, so a new method was devised—the adhesion chamber method—by Rokstad. This consisted of a celluloid chamber resembling a hollow ground slide used in studying hanging drops. The substance to be tested was placed in the well of the chamber and applied to the skin with slight pressure in such a manner that there was no air cushion left in the chamber. Over this was placed a plaster which had a hole in the center corresponding to the top of the chamber. This plaster was used to fix the chamber to the skin. The ordinary patch tests were used to test the eczematous properties of the terpenes.

The toxic effects began to appear when the concentrations reached 30 per cent and increased in frequency and strength in direct proportions to the increase in concentration. One hundred per cent of all persons tested reacted to some concentration of the terpene above 30 per cent, revealing the substance to be a primary irritant.

The allergic potential of these substances was demonstrated in concentrations of 0.1 per cent or less. Since all the persons tested were known to be allergic to pinene, positive reactions were expected in all cases. The purpose was to determine how strong the allergenic power of these substances was. Threshold values were established by the investigations on the bases of the smallest concentration of the substance needed just to produce a reaction. It was found that the eczematous responses varied in different persons and in the same persons to different substances. These eczematous responses were considered dependent on previous exposures and experience with the offending substances while the threshold values were true expressions of the allergic potentials of the test substance.

The results of the experiment indicated that delta (3)-carene and limonene had the strongest allergenic power. Next in order came beta-pinene, monocyclic terpenes, alpha-pinene and finally the low boiling impurities.

In comparison of the toxic and the allergenic properties, parallelism was seen only in the low boiling impurities. In the other substances the degree of toxic or primary irritative property was related to the boiling point of the terpene. The reaction to toxic concentrations was considered an expression of the role played by the barrier of the skin.

PARAKERATOSIS VARIEGATA (PARAPSORIASIS VARIEGATA S. RETICULARIS) W. L. L. CAROL, J. R. PRAKKEW and W. STIGER, *Acta dermat-venereol.* **24** 1 (Jan) 1943

Two cases of parakeratosis variegata are described in detail. The condition in 1 of them was originally diagnosed as parapsoriasis en plaque. The true diagnosis became evident when the skin was examined histologically.

The authors found on histologic examination that a mild exudation was usually present, accompanied with some parakeratosis and local atrophy. In the stratum papillare and just below it there was a consistent perivascular round cell infiltration. This infiltration was most prominent around the vessels which ran from the deeper layers of the skin to the surface. Occasionally this infiltrative process reached as far as the cutis. At times the infiltration was not limited to the vessels but was diffuse and localized in the papillary and subpapillary areas.

In this disease the reticular pattern was a constant finding. There were patterns here which had to be differentiated. One was a primary network composed of numerous unaffected islets of sound skin, and the other was a secondary network whose meshes corresponded to the areas of atrophy which replaced the primary papule.

The differentiation made by Civatte between parakeratosis variegata with and without atrophy was rejected because it was thought that atrophy was merely a measure of degree of involvement.

Parakeratosis variegata, although it may still be classed in the parapsoriasis group, is a disease entity and should not be considered a rare final stage of parapsoriasis.

ROBINSON, Washington, D. C.

# Society Transactions

## MANHATTAN DERMATOLOGIC SOCIETY

E W Abramowitz, M D, *President*

Wilbert Sachs, M D, *Secretary*

Oct 9, 1945

A Case for Diagnosis (Scleredema Adultorum? Scleroderma?). Presented by DR E W ABRAMOWITZ

Mrs E L, a woman aged 57, born in Germany, first noted stiffness of the shoulders in 1941. This has gradually spread so that now the neck, chest, arms and thighs present a leathery hardness. The hands and feet are not affected. The disturbance appeared suddenly, with no previous illness or operation except a hysterectomy in 1925.

Since 1941 the patient has received fever therapy, injections of typhoid vaccine and roentgen therapy, without relief. She has had a thorough physical examination at the Mayo Clinic and at the New York Post-Graduate Medical School and Hospital, where electrocardiographic, encephalographic and basal metabolic tests revealed a normal condition.

The patient has been under my observation since June 22, 1945. She is receiving neostigmine, 15 mg two or three times daily, with baking and massage. The skin has at times shown softening, but there has been only slight relief from the choking sensation, difficulty in breathing and interference with free motion of the arms of which the patient complains. Biopsy revealed changes compatible with scleredema.

The patient is presented for suggestions as to treatment.

### DISCUSSION

DR MAX SCHEER: I think a diagnosis of scleredema adultorum can be ruled out, for the following reasons. First, the disturbance did not follow an infectious disease such as influenza or any other infection, and, second, even untreated scleredema spontaneously disappears, usually in a few months, a year or a year and a half. The wide extent of this eruption, the boardlike induration and the absence of erythema, such as is seen in scleredema adultorum, makes it scleroderma, in my opinion.

DR ISADORE ROSEN: I had just the opposite impression of the condition in this case. The skin itself is soft, but the underlying structures are firm, giving the impression of edema, whereas in scleroderma the epidermis itself shows changes which are perceptible to the touch. The changes in the epidermis are lacking in this case. In a process which has lasted so long there should have been changes in the distal portions of the upper and lower extremities. My clinical diagnosis is scleredema adultorum.

DR GEORGE C ANDREWS: Three weeks before the onset of this disease the patient had a severe accident, involving a blow on the forehead and unconsciousness. She was confined to bed and suffered from headaches and dimness of vision. She attributes her present difficulty to that injury. I do not know whether it could have affected the pituitary body or not. All that Dr Scheer says is true. At the same time, I feel that this illness is of long duration for scleredema adultorum. I have never seen a case of scleroderma like this before, or one without more involvement of the skin. The epidermis and dermis are apparently normal. The subcutaneous tissues may be involved, but I feel that the lack of involvement of the hands and feet and the limitation of the disease to the upper part of the body are factors in favor of the diagnosis of scleredema.

DR FRED WISE I am in accord with Dr Rosen and Dr Andrews in their opinion that this case is not one of true scleroderma. The epidermis shows nothing abnormal, but the skin is bound down. I favor the diagnosis of scleredema adultorum, regardless of the duration of the disease in this case.

DR WILBERT SACHS I agree with what the others have said. This case has features of scleredema and also of scleroderma. If one puts them together, one comes to the conclusion that the disease is probably the edematous stage of scleroderma. This would have all the features seen in this patient. One does not know how long it takes for sclerosis to develop in any given case, but eventually it does form.

DR E W ABRAMOWITZ I am in favor of the diagnosis of scleroderma, even if the patient does not show all the classic features of that disease at present. She is getting some relief from neostigmine bromide, given as 15 mg tablets three times a day, this drug causes increased vascularity of the skin. Baking and massage, with warm baths, keep her still more comfortable.

#### A Case for Diagnosis (Poikiloderma Vasculare Atrophicans?) Presented by DR ISADORE ROSEN

H E, a woman aged 48, registered at the clinic of the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital in September 1945, complaining of an eruption of ten years' duration.

On the right upper part of the chest, on both arms, in the axillas, on the lateral aspects of the trunk and over the abdomen, the hips and the inner aspect of the left thigh there are large erythematous and scaly plaques, which on close examination show spots of telangiectasia, pigmentation, depigmentation and atrophy. On both thighs and forearms and the trunk there are round or oval, slightly scaly, brownish lesions varying in size from that of a quarter to that of a silver dollar. These are apparently of recent origin.

Laboratory examinations, including blood and differential counts and urinalysis, gave normal results. Serologic tests for syphilis gave negative reactions.

Biopsy of the affected skin was reported to show mycosis fungoides.

#### DISCUSSION

DR DAVID BLOOM This patient presents two kinds of lesions: the large plaques, showing the features of poikiloderma, and the round or oval lesions, which are slightly raised and brownish. The patient states that the latter lesions are of more recent origin. Both biopsy specimens have been taken from these brownish lesions, which do not yet show the clinical features of poikiloderma; accordingly, the features of poikiloderma are not seen microscopically. In spite of the pathologist's report of mycosis fungoides, the diagnosis of poikiloderma vasculare is to be favored.

DR WILBERT SACHS I saw no evidence of poikiloderma in the slide. The elastic tissue was present. There was evidence of mycosis fungoides, with epithelioid and other type cells. It is interesting that extensive forms of what appears clinically to be poikiloderma often terminate in mycosis fungoides.

DR MAURICE J COSTELLO I think this patient has mycosis fungoides. Some of the nummular lesions show infiltration, and there is a difference in the infiltration in the same and in different lesions. It is not too unusual in cases of mycosis fungoides of long standing to observe plaques which become telangiectatic and undergo atrophy.

DR F W ABRAMOWITZ I recall seeing a patient for whom a diagnosis of parapsoriasis *en plaques disseminées* was made but who had lesions resembling poikiloderma vasculare atrophicans. That patient had received grenz radiation therapy, and the question arose whether the eruption was a secondary radiodermatitis. He later had mycosis fungoides.

DR ISADORE ROSEN Almost every time a patient with this disease is presented there are variations in clinical interpretation. There are lesions in this case which

would fit in with parapsoriasis, and even psoriasis, but on careful analysis the telangiectasia, pigmentation and atrophy in some of the lesions confirm the diagnosis of *poikiloderma*

### Dermatophytosis (Eczematized) Presented by DR GEORGE M LEWIS

M D, a man aged 55, first noted an eruption on his feet over a year ago. He has had considerable therapy from several physicians, beginning with camphorated phenol N F, carrying through with a series of roentgen treatments and including a large assortment of salves, foot baths, and the like. There are periodic exacerbations, the last of which occurred three weeks ago.

Examination reveals an acute, inflammatory dermatitis involving the feet and hands. The affected skin is erythematous and edematous. There are a number of deep-seated vesicles and pustules on the soles and the sides of the fingers. A fading, erythematous, blotchy eruption may be observed on the thighs and legs below the knees.

Culture on August 15 was negative for fungi.

#### DISCUSSION

DR MAURICE J COSTELLO I should like to suggest that this patient be given patch tests of the inner sole and lining of his shoes. It is possible that the dye of the leather shoe lining is the cause of his eruption.

DR ISADORE ROSEN I agree with Dr Costello that the patient has a contact dermatitis rather than an eczematized dermatophytosis. Every now and then one sees a patient with cutaneous manifestations which clinically suggest dermatophytosis but which on careful examination are more diffuse and involve larger areas than are ordinarily seen in dermatophytosis. Occasionally one sees a bullous eruption closely resembling the bullous type of erythema multiforme, with extensive involvement of other parts of the body, as a result of sensitivity to leather dyes. For the patient under discussion, I should advise changing to canvas shoes for a while and using local bland treatment. I should also suggest patch tests.

DR GEORGE C ANDREWS Last winter I worked on 2 cases of this kind, I performed patch tests to leather and shoe linings, and some of the tests gave strongly positive reactions. One patient was in the office recently, apparently well, but he had an experience a few months ago which was interesting. He carried a leather pocketbook in his right hip pocket and got a patch of dermatitis on the right buttock, which he could not explain. As soon as he stopped wearing his pocketbook in his hip pocket the dermatitis disappeared. One of the men who worked with me on those cases has written me since that in similar cases he has taken hematocrit readings, found a macrocytic anemia and administered crude liver extract and pyridoxine, with great benefit.

DR E W ABRAMOWITZ I had a patient with dermatitis of the feet that resulted not from the shoes themselves, but from an ointment containing sulfanilamide which got into the shoes.

DR GEORGE M LEWIS Cases such as this are common enough, so that every one has had experience with the difficulty of managing them. Since my report on shoe leather dermatitis (*Dermatitis Venenata Due to Shoe Leather*, *ARCH DERMAT & SYPH* 24 597 [Oct] 1931), I have observed many instances of proved contact dermatitis from shoe leather, but none resembling the case under discussion. However, I shall make patch tests to be certain. It would seem that the first eruption was a tinea infection, the fungi have probably been killed, but, as so many do, the patient has acquired a high sensitivity of the skin. Whereas fungi do not grow well on eczematized skin, the converse is true, and in the infection due to *Microsporum gypseum* one frequently sees a superimposed eczema or dermatitis. This patient has several known sensitivities, including a pronounced reaction to salicylic acid. He undoubtedly rubs and scratches into his skin a large number of pyogenic organisms. Cases such as this may become complicated, and their management is often difficult. At present the patient is using bland powders.

and pastes I think one has to be careful in the use of roentgen rays, ultraviolet rays, oidiomycin and all strong topical remedies

### **Carotenemia** Presented by DR THOMAS N GRAHAM

M S a woman aged 21, born in the United States, was first seen by me on September 28 She complained of a discoloration of four years' duration involving her palms and soles She stated that she and her mother had been drinking large quantities of carrot juice since before the onset of the eruption They had been told that carrot juice was beneficial to the eyes

There is a yellowish pigment of the palms and soles Examination of the patient's mother showed a similar, but less pronounced, eruption

It has not been possible as yet to have blood tests for carotene or urinalysis for carotenoid pigment

### **A Case for Diagnosis (Neurodermatitis—Hypertrophic or Tumid Type?)**

Presented by DR ISADORE ROSEN

Mrs A O, previously presented before the New York Academy of Medicine on Jan 2, 1945, is presented again for further discussion

At present the lesions consist of groups of raised, slightly infiltrated papules, which under the microscope are undoubtedly vesicular The eruption is now most profuse on the flexor surfaces, anteriorly and laterally, of the upper extremities, extending downward toward the hands, where the eruption is on the extensor surfaces The eruption on the chest consists of lesions which are fused, forming a large plaque covering the entire sternum The abdomen is fairly free, and so is the back The eruption on the lower extremities involves the inner surfaces of the thighs, where the characteristics are similar to those on the upper extremities

The main complaint is itching and burning, although there are no clinical evidences of scratching

This patient has been observed for three years, during which time the lesions have not changed in the slightest, except that in certain areas they have disappeared She has had various types of treatment, both internal and external, including roentgen irradiation, without any effect on the lesions

During the past two or three months the patient has gained 5 pounds (2.3 Kg) in weight and looks much better than she ever did The patient states that she feels best when at the seashore, taking ocean baths and sun-bathing During cold weather her symptoms are greatly aggravated

### **DISCUSSION**

DR FRED WISE I agree with the diagnosis as presented Cases of this kind are described and illustrated in Jadassohn's "Handbuch" under the name of neurodermatitis circumscripta hypertrophica

DR WILBERT SACHS I studied the slides in 2 biopsies and could not make a diagnosis of mycosis fungoides One can put this process in the neurodermatitic group The cells are all of one type, plasma cells, and they are focal about the vessels I know of another case exactly like this in which the diagnosis of mycosis fungoides was made many times The lesions were always pure plasmomas, and roentgen therapy gave little or no relief I believe that this eruption is a distinct entity which belongs in the neurodermatitic group and is not related to mycosis fungoides

DR ANTHONY C CIPOLLARO I treated this patient at the Skin and Cancer Unit with roentgen radiation It is generally known that mycosis fungoides responds extremely well to irradiation This patient did respond, but not well, and I think that the therapeutic test is in favor of the diagnosis of neurodermatitis and against that of mycosis fungoides

DR GIRSCH D ASTRACHAN I observed in the Metropolitan Hospital a case of generalized neurodermatitis with large areas of swelling and hypertrophy of

the skin and lesions similar to those we saw tonight. I agree with Dr. Rosen's conception of this case.

**DR ISADORE ROSEN** This case was previously presented as "a case for diagnosis (mycosis fungoides?)," and almost all the members present suggested the diagnosis of mycosis fungoides. I can readily see how that diagnosis would have to be seriously considered from one examination. This case has been studied from many angles, including pathologic examination, but none of the observations fitted in with the diagnosis of mycosis fungoides. The lesions are tumid and highly pruriginous, and occasionally there is a serous exudate from the surface. At no time have they ulcerated or formed tumors. They are symmetrically distributed and resistant to all forms of therapy, including roentgen irradiation.

#### **Chronic Lymphedema of the Eyelids.** Presented by **DR DAVID BLOOM**

**S M**, a woman aged 73, came to the clinic of the Skin and Cancer Unit of the New York Post-Graduate Hospital on July 2, 1945, complaining of swelling of the eyelids, which has been present for the past two years.

The skin beneath both eyes is severely edematous, forming a walnut-sized bag. The upper eyelids are similarly affected, but to a less degree. The consistency of the swellings is of a gelatinous, cystic quality, being firmer on the left than on the right. The skin overlying the swellings is normal in color.

The patient denies any preceding disorder of the skin or underlying tissues in the area of the eyes or face.

The erythrocytic sedimentation rate was normal. The red and white blood cell count and the differential count gave normal values, but the color index was above 1. The urine was normal, and the Wassermann reaction of the blood was negative.

Examination of the nose and throat failed to reveal any abnormality.

#### **Pityriasis Rubra Pilaris.** Presented by **DR JACK WOLF**

**F L**, a woman aged 26, is presented from the Skin and Cancer Unit of the New York Post-Graduate Hospital with an eruption on the face, hands and forearms of two or three months' duration. She states that she had a similar eruption on the forearms once before, which healed spontaneously.

On the nose the patient presents a somewhat larger than pea-sized, brownish, dry, rough, flat and barely elevated, circumscribed lesion with enlarged follicular orifices. There is diffuse bluish pigmentation of the face, chiefly in the zygomatic regions. The dorsal aspects of the proximal phalanges of all the fingers are profusely covered with small, red, papular lesions, each pierced by a central hair. The lower half of each forearm, chiefly on the flexor surfaces but also extending posteriorly, is profusely covered with pinhead-sized, flat, erythematous papules, slightly raised above the level of the surrounding skin.

#### **DISCUSSION**

**DR E W ABRAMOWITZ** There are some clues that might help, the pigmentation of the face and the follicular plugging on the forearms may be due to the use of a fatty preparation in these areas.

#### **Periadenitis Mucosa Necrotica Recurrens Aphthous Stomatitis?** Presented by **DR THOMAS N GRAHAM**

**A I**, a man aged 26, born in Italy, was first seen at New York Hospital on September 14. He complained of recurrent ulcers of two and one-half years' duration involving the tongue and buccal mucosa. He states that the lesions have been extremely painful and take from one to two months to heal, and that they are preceded by a lump under the mucous membrane. Since the onset of the eruption a new ulcer has appeared approximately every three weeks. There is no history of syphilis.

Examination shows punched-out ulcerations on the tip of the tongue and on the buccal mucosa on the left side. There are also a number of scars from previous lesions.

The Mazzini test of the blood was negative. Smears were negative for Vincent's organism. The blood count showed 13 Gm of hemoglobin per hundred cubic centimeters, 5,100,000 red cells and 11,600 white cells. The differential count was essentially normal.

The patient had previously been treated with inoculations for smallpox and vitamin therapy. Since he has been under the observation of the presenter he has received two roentgen treatments of 75 r each at intervals of one week, he has been using an antiseptic mouth wash and has taken large doses of a vitamin B preparation. There has been no improvement in his condition.

### Erythema Elevatum Diutinum Presented by DR MAURICE J COSTELLO

J H, a man aged 72, from the dermatologic wards of Bellevue Hospital, was previously presented by Dr David Bloom before this society in January 1938 (ARCH DERMAT & SYPH 37 918 [May] 1938) with the diagnosis of possible lymphoblastoma or xanthoma, and was again presented by him before the May 1938 meeting as having erythema elevatum diutinum (ARCH DERMAT & SYPH 39 369 [Feb] 1939). The patient was presented before other dermatologic societies, as indicated in the second reference. He is presented again to demonstrate the persistence of the eruption, the changes which have occurred in the lesions, some of which have undergone involution, and the progression of the disease, as evidenced by the appearance of plaque-like tumors. The patient has had no constitutional symptoms and has been in good health in spite of an extensive dermatosis.

### DISCUSSION

DR WILBERT SACHS This case is interesting in view of the idea that there are two types of erythema elevatum diutinum. One is an atypical variety of granuloma annulare, with lesions similar to those presented by this patient. The other is a perivascularitis, as described by Weidman, in which the walls of the blood vessels are broken and about them are many polymorphonuclear leukocytes. Dr Weidman performed the biopsy in this case, and it would be interesting to know which of the two types of processes he found, for clinically the lesions do not appear like the form he described.

DR FRED WISE The lesions conform more closely to those of extracellular cholesterosis than to those of erythema elevatum diutinum. May I suggest that scarlet red stain be used when a fresh section is prepared?

DR WILBERT SACHS If this were the type that Weidman reported, I cannot understand how the lesions could become so large and fungating. There would have been so much change in the vessels that the entire lesion would have become necrotic and broken down.

DR MAX SCHEER The lesions on the buttocks, which I understand are fairly recent, look clinically like granuloma annulare.

DR MAURICE J COSTELLO The lesions on the hands have changed greatly in the last seven years. I last saw the patient four years ago. At that time the lesions on the back of the hands resembled those which are seen on the buttocks this evening. I presented a patient before this society last year with a diagnosis of possible Kaposi's sarcoma, which was later shown to be erythema elevatum diutinum. Several of the members suggested the diagnosis of xanthoma tuberosum multiplex because the lesions were confined to the backs of the elbows and knees. During the period of seven or eight months that the patient was under observation in the ward there was no change in the lesions, but later they suddenly began to ulcerate. Frequent attacks of erythema-multiforme-like lesions then developed on the hands, feet and neck, independently of the other lesions.

## NEW ENGLAND DERMATOLOGICAL SOCIETY

Bernard Appel, M D, President

G Marshall Crawford, M D, Secretary

Boston, Oct 10, 1945

## Sarcoidosis of the Skin Presented by DR WILLIAM R HILL JR, Boston

The Reverend Sister E, aged 45, had noted the gradual development of nodules under the skin of the trunk and extremities during the past eighteen months. The skin overlying some of these nodules became discolored. No history of injury to these areas was obtained. The patient had no systemic complaints, and her general health had been excellent. She denied experiencing excessive fatigue or having had loss of weight or minor infections. There was no family history of cutaneous disease.

Examination discloses numerous nontender subcutaneous nodules on the trunk and the extremities. These are from the size of a pea to that of a cherry and are not symmetrically distributed. They are distinctly indurated. The skin is normal over some lesions and assumes a bluish red color over others.

A biopsy had been performed, and the slide was at hand. No other data were available.

## DISCUSSION

DR WALTER F LEVER, Boston. The histologic section is consistent with a diagnosis of sarcoid. This case is interesting because of the presence of both cutaneous and subcutaneous lesions. The clinical diagnosis could therefore be Darier-Roussy sarcoid. After a review of the literature on Darier-Roussy sarcoid, it seems to me that this variety does not represent an entity and that the cases described under this head can be assigned to three: (1) Boeck's sarcoid, (2) erythema induratum and (3) Weber-Christian disease (nodular nonsuppurative panniculitis). In the present case the section suggests Boeck's sarcoid with subcutaneous location. I believe that this patient should be thoroughly studied for involvement of the lymph nodes, tonsils, lungs, spleen, liver and phalanges.

DR JACOB H SWARTZ, Boston. I think the diagnosis is sarcoid but should like to see sarcoma ruled out.

DR FRANCIS P MCCARTHY, Boston. I did not see this patient but examined the pathologic section. The slide revealed changes deep in the subcutaneous layer. The presence of giant cells and epithelioid tissue and the pronounced cellular reaction were consistent with sarcoid. Nothing in the picture suggested sarcoma.

## A Case for Diagnosis (Eczema? Carcinoma Simplex of the Nipple?)

Presented by DR LEO KORETSKY, Chelsea, Mass

M C S, a 23 year old white housewife, was presented with an eruption on both breasts of two years and three months' duration. The eruption began about the nipples and gradually extended peripherally. The patient has been treated in several clinics, without relief.

The nipples and areolas of both breasts present an erythematous eruption with fissuring, oozing and crusting. This extends in a wide band down to the subcostal region on each side. The eruption is sharply defined at the margins. The left nipple is inverted.

A roentgenogram of the chest was normal. The Hinton reaction of the blood was negative. The urine was normal. The blood sedimentation rate was normal.

## DISCUSSION

DR CLARA P FITZGERALD, Worcester, Mass. This eruption might be due to rubber in the patient's brassiere.

DR JACOB H SWARTZ, Boston. This patient has a lesion on the right thigh as well as on both breasts. The lesion on the thigh is not the same in appearance

as those on the breasts and might be the original infection. It is a scaly, papular eruption and seems to have extended peripherally. The lesions on the breasts appear to be less active in the center, and the borders are slightly elevated. This appearance seems to be perfectly consistent with an infection with *Trichophyton rubrum* or *Trichophyton purpureum*. I suggest microscopic and cultural studies before one looks for anything more serious.

DR MAURICE J STRAUSS, Boston. I cannot agree with Dr Swartz that the central portions of these lesions are inactive. There is a great deal of oozing in those areas. The question of carcinoma simplex of the nipple has been raised. If this woman has had carcinoma of the nipple for over two years, it is probable that there is carcinoma of the mammary ducts by now. Therefore, if consideration is given to this diagnosis, there should be no further temporizing. A biopsy should be performed at once.

DR BERNARD APPEL, Lynn, Mass. Would you suggest that the nipple itself be included in the biopsy?

DR MAURICE J STRAUSS, Boston. I think the specimen should be taken deep enough to include some of the ducts.

DR WALTER F, LEVER, Boston. A strong point against the diagnosis of carcinoma simplex of the nipple is the bilateral nature of the eruption.

DR LEO KORETSKY, Chelsea, Mass. Rare cases of bilateral carcinoma simplex of the nipple have been reported.

DR JOSEPH MULLER, Worcester, Mass. This eruption began at the time the patient was nursing her baby. A great deal of treatment has been prescribed, as well as much self treatment. Before performing a biopsy, one should try to heal the irritation resulting from therapy and keep her on a regimen of bland applications. This might not be anything more than a dermatitis from overtreatment.

DR FRANCIS M THURMON, Boston. I have followed a similar case for two years. The nipple was inverted during that time, but in the present case the inversion has been of only two months' duration. The dermatitis on the breasts and in the axillary folds appears to be of contact origin, from medication. Secondary mycotic infection might lead to development of a lesion on the thigh. The question in my mind is: Can persistent irritation over a period such as this, whatever the cause, produce carcinoma?

DR FRANCIS P MCCARTHY, Boston. I think this case deserves histologic study. It should include part of the nipple and will show whether this patient has carcinoma simplex of the nipple. There are two schools of thought regarding the development of this disease. One holds that it is a primary dermatitis with secondary development of carcinoma of a specific type involving the skin. The other predicates a primary adenocarcinoma of the ducts, with extension into the skin. Has the patient had roentgenologic treatment?

DR BERNARD APPEL, Lynn, Mass. No.

DR FRANCIS P MCCARTHY, Boston. In that case she is one of the few with an eruption of this type who has gone on such a length of time without receiving it. In this instance the pendulous breasts should be kept elevated to relieve vascular congestion. This might be helpful in treatment.

DR BERNARD APPEL, Lynn, Mass. What is your experience, Dr McCarthy, with specimens taken from the nipple? It is my understanding that taking a biopsy specimen from that location must be executed with considerable caution. Some surgeons prefer complete excision.

DR FRANCIS P MCCARTHY, Boston. If a biopsy specimen is removed from the nipple, one can obtain a portion of the duct and also have a representative piece from the integument.

DR LEO KORETSKY, Chelsea, Mass. My colleagues and I have followed this case in our clinic for four months. It was decided to present the patient today, before using roentgen therapy. Since the question of a malignant growth has been stressed, we shall carry out a biopsy before using any radiation.

**Squamous Cell Epithelioma of the Ear** Presented by DR C GUY LANE, Boston

J S, a 66 year old white laborer, was presented with a lesion involving the left ear and temporal region. Fifteen years ago the patient was struck on the left ear with an umbrella and had an ulcer about 2 cm in diameter directly in front of the ear. This did not heal for two or three years. Later, the same area was struck with a baseball and ulceration recurred. Until four years ago the disease spread progressively, involving the upper half of the ear. Four weeks ago he began to use sulfathiazole ointment, with resultant rapid increase in size of the lesion and almost complete undermining of the external ear. The patient has lost 20 pounds (9.1 Kg) in the past year and is practically deaf in the affected ear.

The site of the left ear shows an ulceration about 7 by 11 cm and perhaps 3 cm deep at the point of greatest depth. This area is covered with bright red granulation tissue, and there is considerable oozing when the dressing is removed. When the patient was first seen, two weeks ago, about one third of the lower portion of the ear remained, minus the lobe. This remnant was dusty purple, moderately indurated and had an adherent crust at the upper and lower edges. It was attached to the side of the scalp by a pedicle 3 cm in width. As he is seen today, the remnant of the ear is gone.

Two weeks ago the remnant of the left ear was removed surgically. Histologic examination of the specimen revealed epidermoid carcinoma grade III.

Several roentgen treatments have been administered, but only as a palliative measure.

DISCUSSION

DR FRANCIS P MCCARTHY, Boston. Has there been metastasis to the regional lymph nodes?

DR C GUY LANE, Boston. This is an interesting example of the possible serious portent of a relatively insignificant lesion. The history is that of a minor localized lesion in front of the ear which gradually extended. The patient came to the clinic only when his disease began to reduce the hearing of the left ear. It took a great deal of persuasion even then, on the part of his son, a priest, and the rest of the family, to get him to his local physician. When he was first seen, the remnant of the ear was hanging by a small pedicle at the lower end. The ulceration revealed pearly borders all around the edge. I have never seen a lesion in which one could insert the finger so deep into the head without touching the brain.

DR BERNARD APPEL, Lynn, Mass. Was there any evidence of metastasis?

DR C GUY LANE, Boston. There was no suggestion of involvement of the lymph nodes.

**Hidradenitis Suppurativa** Presented by DR WALTER F LEVER, Boston

M M A, a white woman aged 45, has had ulceration and formation of fistulous tracts in the perineal region for four years. Three years ago there was temporary improvement following an operation for anal fistula and ultraviolet irradiation. Two and one-half years ago the lesions extended to the intergluteal fold and the inguinal regions. The patient was hospitalized for six weeks in 1943 and improved under treatment with sulfonamide compounds and fractional roentgen irradiation, the total dose amounting to 600 r. After this, the disease remained fairly quiet until about three months ago. Two months ago she was readmitted to the hospital because the ulceration and exudate from the perineal lesions became more severe and a new lesion with purulent exudate had appeared on the left buttock. The affected areas do not itch or cause pain.

There are large ulcerative lesions in both inguinal areas, the intergluteal fold and the perineum, with deep sinuses draining purulent exudate. The left labium majus is perforated and cordlike. The perineum is partially destroyed, and practically no external sphincter remains.

*Laboratory Findings*—The tuberculin test gave a positive reaction in a dilution of 1:10,000, the Frei test gave a negative reaction, the Hinton reaction of the

blood was negative, guinea pig inoculation gave a negative result for tuberculosis (twice), the staphylococcus agglutinin titer was zero, cultures yielded *Staphylococcus aureus* and *Proteus vulgaris*. Two large excisions were taken for biopsy. Both sections showed acute and chronic inflammation, granulation tissue with foreign body giant cells and areas of necrosis.

Treatment has consisted of sitz baths of potassium permanganate, painting with 1 per cent basic fuchsin, vinegar douches, administration of 500 mg of ascorbic acid daily and intramuscular injection of 12,000 units of penicillin every three hours. Oral administration of sulfadiazine has just been started.

#### DISCUSSION

DR MAURICE J STRAUSS, Boston. Most such patients have axillary lesions, but there is none present in this case, a feature which seems unusual to me. I should appreciate suggestions for therapy.

DR FRANCIS M THURMON, Boston. I think these lesions will clear up with topical applications of a sulfonamide powder and moist dressings of a sulfonamide solution. This treatment may be supplemented with oral administration of one of the sulfonamide drugs.

DR JACOB H SWARTZ, Boston. The only case in which I have seen the lesions clear up was one in which a radical surgical excision was done. This would be a big job in the present case, and several surgeons have refused it. In my 1 private case, with involvement of the axillas, the upper part of the back and the buttocks, cure was effected by radical excision of the various areas at different times.

DR JOSEPH MULLER, Worcester, Mass. I know of no case of hidradenitis in which a cure has really been produced. The lesions will improve considerably with the use of penicillin and sulfonamide drugs, but these drugs merely clear up the secondary infection.

DR FRANCIS M THURMON, Boston. The laboratory work-up of this case did not indicate any studies for Donovan bodies.

DR WALTER F LEVER, Boston. Several attempts were made to identify these organisms in the histologic sections, but none were seen.

DR FRANCIS P MCCARTHY, Boston. Was there a typical picture of cystic apocrine glands?

DR WALTER F LEVER, Boston. The two histologic specimens, unfortunately, represented only the late stage of the disease. No eccrine or apocrine glands were present, only granulation tissue with foreign body cells and areas of necrosis were seen.

DR JOSEPH BECKER, New London, Conn. I have been fortunate in seeing at least 6 cases of hidradenitis, in 2 of which the lesions were in the axilla and in the others in the groin. In all these cases tremendous quantities of penicillin and sulfonamide drugs and combinations of the two were given. There was no apparent result. Surgical measures were carried out in 2 cases, followed by plastic repair, but intervention was not extensive, in both cases there was recurrence.

DR G MARSHALL CRAWFORD, Brookline, Mass. I can duplicate Dr Swartz's case in which cure was effected by radical surgical intervention.

DR E MYLES STANDISH, Hartford, Conn. I have known of similar results in 2 cases.

DR CHARLES N SULLIVAN, New Britain, Conn. How about using zinc peroxide in paste form?

DR WALTER F LEVER, Boston. This patient will now be treated with a combination of penicillin and one of the sulfonamide compounds.

**Pyoderma Gangrenosum** Presented by DR C GUY LANE, Boston

S K., a Polish Jew aged 63, a bricklayer by occupation, for about eighteen years has had recurrent chronic ulcers of the chest and both legs. The lesions have

been extremely resistant to treatment and after healing in one location soon appear elsewhere. They begin as small red areas, which soon become eroded and ooze a serosanguineous fluid.

At the time of admission to the hospital, three months ago, this patient exhibited two large, crater-like ulcerations on each thigh, measuring about 10 by 15 cm. The bases of these lesions were granular and covered with a loose yellow crust. Several smaller similar lesions were present on each leg. The medial aspects of the thighs and legs showed old serpiginous scars. There were several similar scars on the chest. Since his admission, several more ulcers have developed above and below the knees and have extended peripherally, with undermined edges. At this time all lesions are healed.

Examinations of the blood and urine have repeatedly given normal results. The Hinton reaction of the blood was negative. Cultures have shown *Escherichia coli*, *Staph aureus* and beta hemolytic streptococci. No fungous organisms were obtained. A biopsy specimen revealed only acute and chronic inflammation.

Local treatment has consisted of chlorinated soda dressings, zinc peroxide paste, 1 per cent basic fuchsin paint and penicillin ointment. The patient has received large doses of vitamin A and ascorbic acid. He was given 40,000 units of penicillin intramuscularly every three hours, to a total of 16,400,000 units. He has also received 6 Gm of sulfadiazine daily for the past thirty days, in conjunction with the penicillin.

#### DISCUSSION

DR C GUY LANE, Boston. It is unfortunate that I did not have photographs on exhibit showing the condition of the patient when he was admitted. The scars of old lesions and the ulcerating granulomatous areas on the thighs suggested blastomycosis, or possibly some of the unusual manifestations of sporotrichosis. I watched several new lesions develop. They began with erythema, followed by some infiltration and then ulceration. The edges continued to break down as the lesions spread. Material from an area on the left knee was aspirated before ulceration, but the pus was sterile. That lesion healed without going on to ulceration, I do not know why. There was improvement with penicillin alone, without complete healing. For a time the patient was given potassium iodide but he became steadily worse. Of the several forms of local therapy, penicillin ointment was found to be the best. It was remarkable to watch the healing of all lesions when penicillin and a sulfonamide drug were administered together.

DR JACOB H SWARTZ, Boston. Did this man show glycosuria or hyperglycemia? Some of the patients with these lesions have been diabetic. I should like to submit another diagnosis for the sake of discussion: dermatitis nodularis necrotica. The fact that lesions were apparently sterile before breaking down suggests that possibility. The disease frequently occurs on the lower part of the trunk, although this man had lesions on the breasts.

DR WALTER F LEVER, Boston. I have recently read a case report by Miescher (*Dermatologica* 91 226, 1945). The clinical description and the photographs are strikingly similar to those in this case. Bacteriologic studies in Miescher's case revealed *Staphylococcus aureus haemolyticus*. Oral sulfonamide therapy and electrocoagulation resulted in healing. Miescher's diagnosis was pyoderma serpiginosum gangrenosum.

#### Herpes Gestationis Presented by DR C GUY LANE, Boston

A M., a white housewife aged 38, has a widespread eruption of four months' duration. This began during the sixth month of pregnancy. It started with groups of tapioca-like vesicles on both forearms. Within a few weeks the patient noticed the appearance of a blotchy red, itching eruption on all extremities. Within the past two months groups of blisters have appeared on these regions, with increased itching and burning, some have occurred also on the trunk. These have come and gone to a certain extent. There was one complete remission of short duration two months ago. Three weeks ago the patient was delivered of a normal infant. The

dermatitis persisted and has become steadily worse. She was admitted to the Massachusetts General Hospital ten days ago. Shortly afterward ligation of the saphenous vein was performed bilaterally because of thrombophlebitis.

There is a bullous eruption on all this patient's extremities, most severe on the arms. The lesions vary from 0.5 to 2 cm in diameter. There is a distinct tendency to group arrangement. The bullae are fairly thick walled, tense and filled with clear fluid. Pigmentation is present in varying degrees on the extremities and at the site of healed lesions, especially on the thighs. The crural and pubic regions show similar changes. There are also many groups of small red papules interspersed with vesicles on the extremities, and some of these are excoriated. The forearms and wrists show mild lichenification. On the neck and the lower portion of the back are a few groups of lesions of the erythema iris type. The mucous membranes are unaffected.

The nonprotein nitrogen, total protein and calcium contents of the blood were normal. The urine was normal. The red blood cell count and the hemoglobin concentration were normal. The white blood cell count was 10,400, with 17 per cent eosinophils.

Treatment has consisted of general supportive measures, sedation, administration of calcium by mouth, autohemotherapy and oatmeal baths. There has been steady improvement since her admission.

#### DISCUSSION

DR C GUY LANE, Boston. This patient was presented because of the unusual multiformity of the lesions.

DR JACOB H SWARTZ, Boston. I saw this woman in my office two weeks after she gave birth to her child. At that time there were extensive pemphigoid lesions together with lesions resembling dermatitis herpetiformis. A few were hemorrhagic, and the patient was rather uncomfortable. I do not believe that calcium or autohemotherapy has produced the improvement. It is time for her to get better spontaneously, after childbirth.

DR BERNARD APPEL, Lynn, Mass. Does any one know whether the baby had lesions?

DR JACOB H SWARTZ, Boston. There were no lesions on the baby.

DR WILLIAM P BOARDMAN, Boston. The multiformity of lesions in dermatitis herpetiformis and herpes gestationis is one of the characteristics of these diseases. These diagnoses are hardest for the student in the presence of papular lesions. Somewhere he will find vesicles.

DR WALTER F LEVER, Boston. In toxic eruptions of pregnancy one may find lesions resembling dermatitis herpetiformis, erythema multiforme and pemphigus. In this patient all three types of lesions were present, but those that simulated the lesions of dermatitis herpetiformis were in the majority.

DR JOSEPH BECKER, New London, Conn. I should like to ask whether sulfapyridine has been tried with this patient.

DR JACOB H SWARTZ, Boston. Not with this patient, but in 1 case Dr Lever and I tried sulfapyridine and it was not effective, as in dermatitis herpetiformis. We felt that this patient did not need it.

DR WALTER F LEVER, Boston. In some cases of herpes gestationis recorded in the literature sulfapyridine controlled the eruption, in others it did not. In our case it did not. It is possible that herpes gestationis has more than one cause.

**Nevus Linearis, Localized Scleroderma? (Morphea)** Presented by  
DR BERNARD APPEL, Lynn, Mass

J S., a Negro girl aged 10 years, was exhibited with a lesion on the anterior surface of the left shoulder and the flexor surface of the left arm and forearm of three years' duration. The upper portion of this lesion appeared first in the form of increased pigmentation. This progressed distally in a bandlike streak and finally reached the wrist.

On the flexor surface of the left arm there are macules of depigmented skin, surrounded by hyperpigmentation. The middle third of this arm exhibits an area of indurated, atrophic, white tissue, about  $1\frac{1}{2}$  by 4 inches (3.8 by 10 cm). Distal to this there is a band of hyperpigmented skin extending down to the wrist, with an interruption on the lower third of the forearm.

A biopsy was performed five months ago, and the pathologic report was scleroderma. No treatment has been given.

#### DISCUSSION

DR MAURICE J STRAUSS, Boston. The linear lesion extending down the arm below the frankly sclerodermatous area is edematous and clinically consistent with an early stage of scleroderma. This lesion has not been present throughout the patient's life but has appeared recently. I believe that the entire change is scleroderma.

**Dermatitis Seborrhoeica** Presented by DR WALTER F LEVER, Boston

T Q, a mulatto woman aged 41, has had a generalized eruption of three years' duration. She has been admitted to the Massachusetts General Hospital three times since 1942. Improvement occurred with each admission, but the patient has never been entirely free from the lesions. The present, severe generalized exacerbation began two months ago. Recently dacryocystitis of the left eye developed, which became so severe that she was admitted to the Massachusetts Eye and Ear Infirmary.

Three weeks ago examination revealed a generalized erythematous, oozing, crusting dermatitis which was most severe on the extremities, crural areas, scalp and ears. There were some lichenification and extensive excoriation of the upper extremities. Today there is no exudation and only mild erythema, the lichenification and but few excoriations remain. The dacryocystitis is considerably improved.

Examination of the blood revealed mild secondary anemia. The urine gave a 1 plus reaction for albumin. The patient has been treated for the past four days with a combination of 12,500 units of penicillin by injection every three hours and 3 Gm of sulfadiazine daily given orally. Within four days the patient's dermatitis has improved almost 80 per cent. She is still hospitalized in the ophthalmologic service and has received no local treatment for her dermatitis. This case is presented because of the remarkable response to penicillin.

#### DISCUSSION

DR FRANCIS P MCCARTHY, Boston. Since seborrheic dermatitis is the first cousin of psoriasis, I should like to know whether Dr Lever has had an opportunity to use penicillin in cases of generalized psoriasis.

DR FRANCIS M THURMON, Boston. Penicillin is not effective in the treatment of psoriasis.

DR JACOB H SWARTZ, Boston. I have given penicillin by enema and parenterally, and it was not effective in treatment of widespread psoriasis or exfoliative psoriasis. The good results in this case are due to the effect of penicillin on the bacterial infection, and not on the seborrheic dermatitis.

DR WALTER F LEVER, Boston. On admission this patient presented a generalized eruption, most pronounced in the seborrheic areas. There were extensive areas of oozing and crusting, suggesting a bacterial dermatitis. The combination of seborrheic and bacterial dermatitis has been described by French authors and is referred to by some as the Darier-Ravaut-Ramel type of seborrheic dermatitis. I believe that the bacterial dermatitis is a secondary phase, occurring in the seborrheic areas in cases of severe seborrheic dermatitis. Penicillin in this case controlled the bacterial dermatitis. I do not expect penicillin to cure ordinary seborrheic dermatitis.

DR BERNARD APPEL, Lynn, Mass. Do you care to add anything about the condition of the eye? Was that purely dacryocystitis? Does it have any particular bearing on this case?

DR WALTER F LEVER, Boston It was a purulent dacryocystitis The infection of a tear duct in this case further supports the assumption of a superimposed bacterial factor

**Syphilis of the Skin (Primary, Recurrent)** Presented by DR WILLIAM R HILL JR, Boston

D M, a white truck driver aged 27, was presented with a penile lesion of three weeks' duration This man was hospitalized four months ago with a diagnosis of primary syphilis (glans penis) He was treated with 1,200,000 units of penicillin and discharged when the lesion healed Since that time he has been out of the state and could not be followed He denies having had sexual contact since his discharge from the hospital, four months ago Three weeks ago the penis became irritated and began to swell, and an ulcer recurred at the site of his original lesion The prepuce became swollen, and two crusted lesions appeared at the base of the penis The patient was readmitted to the hospital in this condition The ulcer on the tip of the glans could barely be seen because of edema Extreme tenderness prevented extensive examination There was considerable purulent exudate Nonmatted, tender inguinal nodes were present bilaterally Three dark field examinations for spirochetes gave negative results The urine was normal The Hinton reaction of the blood was negative Penicillin therapy was resumed, with a dose of 40,000 units every three hours, to a total of 2,400,000 units

At this time the edema of the prepuce has subsided and the ulcer partially healed It is still rather tender, and there is some exudate

DISCUSSION

DR AUSTIN W CHEEVER, Boston It is interesting that this lesion should appear at exactly the same place as the other one This might be a chancre, but the patient had a negative Hinton reaction and a negative dark field Secondary infection has been suggested Except for chancre redux, has any one seen secondary infection of the penis that would look anything like this? I never have The diagnosis of chancre redux or recurrence due to insufficient penicillin therapy would seem to me to fit this case

DR FRANCIS M THURMON, Boston I believe the results of penicillin therapy in early syphilis have been 80 per cent successful This is a pseudochancre redux, in the presence of a negative dark field I should expect the serologic reaction to be positive Lesions of pseudo chancre redux have taken at least 8 to ten years to appear after treatment for early syphilis I wonder whether that observation will be true with penicillin therapy Does inadequate penicillin therapy step up the course of syphilis?

DR JOSEPH BECKER, New London, Conn This is confusing to me The patient had primary syphilis four months ago He had insufficient penicillin treatment according to present standards Some authors find, as Dr Thurmon pointed out, that it takes eight to ten years for the development of chancre redux This seems more likely a recurrence due to insufficient treatment

DR JOSEPH MULLER, Worcester, Mass On the flanks one sees a roseola Do you think that solves the problem?

DR ALFRED HOLLANDER, Springfield, Mass I propose a lymph node puncture, which, in my experience, should always be done when spirochetes are not found in the lesion I do not think this is a chancre redux

**Mycosis Fungoides** Presented by DR EDWARD A LAFRENIERE, Arlington, Mass

A S, a white woman aged 58, was presented with an eruption of nine years' duration, involving the scalp, face, neck, arms, elbows and midtrunk Since the appearance of the first lesions, new ones have continued to develop and older lesions have regressed Those undergoing spontaneous involution leave areas of the skin

resembling old bruises. A biopsy in 1941 was found to show mycosis fungoides. The patient received roentgen treatment followed by exacerbation. Subsequently, management was with conservative local therapy. The point of presentation is the interesting spontaneous involution of lesions.

The eruption is now to be seen on the scalp, face, neck, trunk and upper extremities, it is sparsely and irregularly distributed over these regions without discernible pattern. The active lesions are nodules and tumors from 1 to 25 cm in size, of varying shapes and elevated as much as 2 cm. They are moderately firm, sharply defined, shiny and salmon colored. The sites of old lesions are denoted by faint, brownish pigmentary deposits.

#### DISCUSSION

DR C GUY LANE, Boston. I think spontaneous involution happens occasionally. I recall 2 or 3 cases in which the patient's disease became resistant to radiation and some irritation followed its use, so roentgen irradiation was abandoned. Afterward, lesions came and lesions disappeared without further therapy. One striking case comes to mind in which bandlike lesions about the width of my finger moved slowly across the side of the chest, leaving apparently normal skin as they passed. Finally the borders ran into another lesion, and they merged. Many queer things can happen.

#### Dermatomyositis Presented by DR C GUY LANE, Boston

M G, a white housewife aged 37, was presented through the courtesy of the medical service of the Massachusetts General Hospital. In October 1943 there developed sudden pain and swelling of the ankles and knees, which lasted one week. The patient had no further symptoms until five months ago, when joint pains recurred in the ankles and soon became generalized. Since that time, pain has been intermittent but progressively more severe. She stated that she had had a temperature of 100 F most of that time. Weakness, loss of appetite, sore tongue and loss of 30 pounds (13.6 Kg) in weight have ensued during recent months. There have been no menstrual periods for the past two months. Some puffiness of the face has developed during recent weeks.

On examination this patient is seen to be somewhat emaciated, but the face is moderately edematous. Her entire skin is dry, rough and pale. The hair is distinctly thinned. The tongue is smooth and red. The muscle structure of the extremities is atrophic, and there is pronounced weakness. There is limitation of the motion of all joints. The fingers are distinctly spindled.

Laboratory findings were as follows. The urine gave a 1 plus reaction for albumin and showed 20 to 30 leukocytes and 5 to 10 red blood cells per high power field, with many granular casts. The blood count revealed 3,120,000 red cells, 102 Gm of hemoglobin and 6,300 leukocytes. A roentgenogram of the chest showed a large globular heart with questionable pericardial effusion and a small amount of pleural fluid. The electrocardiogram was consistent with pericarditis. The biopsy specimen showed "the characteristic picture of dermatomyositis."

#### DISCUSSION

DR C GUY LANE. I thought it would be worth while to have this case presented because it represents a definite early diagnosis. The dermatologic lesions are mild but distinct. Dermatomyositis exhibits a variety of cutaneous lesions, but one seldom sees the early type such as this. The early changes suggest lupus erythematosus. There may be lichen-planus-like lesions, vitiligo-like lesions or increased pigmentation. The first changes may appear conspicuously over the extensor aspects of the joints, especially of the hands, and may eventuate in definite atrophic areas. In some instances the lesions are characteristic of poikiloderma.

DR E MYLES STANDISH, Hartford Conn. Has the patient shown any other cutaneous changes?

DR BERNARD APPEL, Lynn, Mass. There are some pigmentation on the thighs and mild edema of the eyelids.

## BROOKLYN DERMATOLOGICAL SOCIETY

David M Davidson, M D , *President*Seymour M Silvers, M D , *Secretary*

Oct 15, 1945

**Pemphigus Vulgaris** Presented by DR LESSER M FRUCHTBAUM

Mrs V N, aged 36, was seen at the dermatologic clinic of the Long Island College Hospital on Aug. 6, 1945, at which time she complained of a rash of nine months' duration. Prior to the appearance of the present eruption she had been taking medicaments for headaches and hay fever. She stated that since her present illness she has lost 15 pounds (6.8 Kg.)

Examination reveals an emaciated woman, weighing 90 pounds (40.8 Kg.) The mouth, palate, buccal mucosa and tongue are covered with large bullae, varying from the size of a hazelnut to that of a walnut and filled with a red fluid. The upper and lower extremities, especially the hands and fingers, are covered with hemorrhagic bullae and exfoliative lesions. The trunk is covered with similar lesions, but to a less degree.

The Nikolsky sign was positive. The Wassermann reaction of the blood was negative. The urine was essentially normal. The blood count showed 3,260,000 red blood cells, 8.5 Gm hemoglobin per hundred cubic centimeters, 10,950 white blood cells, 55 per cent small and 36 per cent large lymphocytes, 6 per cent monocytes and slight eosinophilia. A roentgenographic examination of the chest revealed a normal condition.

On each occasion of the patient's examination at the clinic there were new crops of hemorrhagic bullae in the mouth and over the trunk and the extremities. On Sept. 24, 1945, examination showed several fresh hemorrhagic bullae on the trunk, tongue and pharynx and dried-up bullae on the hands and fingers. Since that date, for the past three weeks, the patient has received acetarsone for the first three days of each week. She has responded favorably. There are no new hemorrhagic lesions, but occasionally a small clear vesicle is discernible. The patient's well-being has also improved.

Tonight several small vesicles may be seen on her thighs and a ruptured vesicle on the tip of her tongue.

## DISCUSSION

DR JOEL SCHWEIG, New York. I agree with the diagnosis, although there might be some doubt as to the typical features in this case. The future will no doubt determine the correctness of this diagnosis. I wonder whether the presenter has a new approach to therapy which he intends to institute in this case.

DR F. ALMORE GAUVAIN. I do not believe that this is a case of pemphigus. I should be more inclined to think that her general systemic condition is responsible for the eruptions. She has anemia, her skin is dry and scaly over the knees, and is thickened, which is certainly not characteristic of pemphigus vulgaris. I think that the tonic effect of the drug is responsible for her improvement. She has a history of having taken drugs, which may have helped to produce the anemia. I believe that if she were treated for anemia and given intensive vitamin therapy she would respond well.

DR JACOB SKEER. I saw this patient last December at the Cumberland Hospital. She then had numerous bullae, some of which were hemorrhagic, she also had a positive Nikolsky sign, as she has tonight. There were numerous lesions in the mouth and her elbows were covered with a thick crust. At that time the diagnosis of pemphigus was made.

DR C. THOMAS CHIARAMONTE. I think that this is a case of epidermolysis. The patient gives a picture of well-being that is not seen in pemphigus vulgaris with such extensive involvement. The lesions are confined mostly to the sites of pressure, the elbows, knees, ankles, palms and fingers, and her history points to

the diagnosis of epidermolysis. She states that every time she receives the slightest trauma bullae arise at the site of trauma. I have observed 2 or 3 cases of epidermolysis bullosa in which lesions were presented on the tongue, palate and mouth, the fact that she is a Puerto Rican and eats hot, peppery food should account for the lesions in her mouth. Bullae of epidermolysis are not uncommon in the pharynx, esophagus, stomach and intestine. Her anemia and run-down physical condition I believe to be due to undernourishment, resulting from dysphagia.

DR SEYMOUR H. SILVERS: A great deal has been said tonight about new bullae developing at the sites of trauma. However, the patient also has lesions on the trunk, in areas not usually subjected to trauma. I think that in this case one ought not to stress too much the factor of trauma in the differential diagnosis. It is well known that in pemphigus, too, trauma will produce bullae. Therefore I do not think that this fact should be used as a differential sign between pemphigus vulgaris and epidermolysis bullosa.

I feel that the lesions in the mouth are significant in arriving at the diagnosis, and I, therefore, favor the diagnosis of pemphigus.

DR DAVID M. DAVIDSON: I do not believe that this is a case of pemphigus vulgaris. On looking at the patient the first thought that comes to my mind is epidermolysis bullosa. The location of the lesions on the elbows, hands and other points of pressure and the characteristic thin, bluish skin over these areas favor this diagnosis.

DR LESSER M. FRUCHTBAUM: I presented this case, first, because it is a classic example of pemphigus. The patient has numerous bullous lesions on the skin and in the mouth which could not be mistaken for anything else, in spite of the history of use of drugs, which confused the picture. Second, the case is presented to dispel the idea that this disease occurs only in persons of the Jewish race. The patient is a Puerto Rican. Then, too, the lesions seen here are essentially hemorrhagic. Lastly, the patient was presented because of the dramatic response to treatment with acetarsone, although I do not expect a permanent cure.

Some of the discussers favored the diagnosis of epidermolysis bullosa, basing their opinion on the occurrence of many of the lesions at sites of pressure. However, many lesions are present on other parts of the body not pressure points. Then, again, one seldom sees hemorrhagic lesions, particularly in the mouth, pharynx and tongue, in cases of epidermolysis bullosa. Therefore this case is presented as one of pemphigus vulgaris.

#### **Pemphigus Erythematosis (Senear-Usher Type)** Presented by DR MAX LERNER

B I, a Jewish man aged 55, was first seen at the Kings County Hospital Clinic, in the service of Dr C. Thomas Chiaramonte, on Sept 24, 1945, with an eruption of about two years' duration, which began with two "pimples" on the scalp. Salves had been used, without effect. The lesions increased in number, involving the entire scalp, nose, upper portion of the face, ears, chest, arms, abdomen and back, in general following a seborrheic distribution.

On the scalp and back, broad merged areas of erythema and crusts are seen. The forehead is erythematous and moist and has a tendency to vegetate. New lesions are seen as flaccid bullae, about 0.5 cm in diameter. In the past two weeks the patient has become completely bald, and the lesions are oozing serum.

The rash did not respond to boric acid ointment. Vitamins aggravate the eruption but the patient's general health is good.

Urinalysis, made on Oct 5, 1945, showed faint traces of albumin and of sugar. The blood sugar on October 10 was 80 mg per hundred cubic centimeters.

The case is presented for suggestions as to therapy.

#### DISCUSSION

DR JACOB SKEER: The lesions on the trunk appear to be bullous eruptions. What interested me particularly was the butterfly arrangement of the erythema on

the face, which appeared similar to that of lupus erythematosus, although it did not have any of the characteristics of this disease. The scalp seems to be entirely covered with crusts, probably ruptured bullae. I think this case falls into the group of pemphigus and lupus erythematosus that one reads about, Sulzberger and Wise claim to have obtained good results with oxophenarsine hydrochloride ("mapharsen") in cases of lupus erythematosus.

### A Case for Diagnosis (Pityriasis Lichenoides Chronica [Juliusberg]?)

Presented by DR E. ALMORE GAUVAIN

T. L., a married woman aged 30, has had lesions on her hands intermittently for about a year. When she was first seen, there were vesicular lesions of a contact dermatitis on the fingers of both hands. One week later small papulo-squamous lesions developed on the torso, and a diagnosis of early pityriasis rosea was made. The lesions did not progress in size, but there appeared some grouping in ring formation on the body, with rounded papules on the flexor surfaces of both forearms. These were all surmounted by definite scales. Pruritus was not present.

On presentation, there are red, rounded papules on both forearms below the cubital fossae, where they are closely aggregated, becoming more discrete above the elbow. On the body are discrete papules and annular groups of papules, with slight scaling.

#### DISCUSSION

DR C. THOMAS CHIARAMONTE: I agree with the diagnosis as presented. Naturally, the diagnosis of lichen planus comes to mind in seeing a rash such as this. However, the lesions have no suggestion of violaceous color, they are shiny, flat and not umbilicated. The distribution is not typical of lichen planus. There are no oral lesions, but this fact would not negate the possibility of that disease. The only peculiar feature is the presence of a dermatitis in the vicinity of the lesions, which may have been due to medicaments used locally.

DR JACOB SKEER: She seemed to have a peculiar eruption. There were lesions that looked like psoriasis and some that resembled lichen planus. I also examined her mouth for lichenoid lesions. To my inquiry as to whether there was itching she replied in the negative, but stated that recently she has been having sensations of burning. Considering the whole picture, I think this is a lichenoid type of parapsoriasis.

DR JOEL SCHWEIG: I believe that the diagnosis should be left open in this case. All dermatologists experience the same perplexity in dealing with cases of early pityriasis lichenoides chronica. At times the eruption may resemble psoriasis, at others it may look like lichen planus. Tonight, the lesions on the back are typical of psoriasis, with its characteristic symptom of dotted bleeding following the removal of scales. The forearms, however, present lesions of a different type—smooth, raised, glossy, violaceous, they could easily be mistaken for the lesions of lichen planus. All in all, a multifiform picture is presented, with lesions of varying appearance. The disease is most likely to fall into the category of pityriasis lichenoides chronica, a diagnosis which will be verified in the future by its refractory behavior to treatment.

DR DAVID M. DAVIDSON: There are no features characteristic of psoriasis or lichen planus. I think this case is one of parapsoriasis.

DR F. ALMORE GAUVAIN: This case has been presented for diagnosis, with a tentative diagnosis of pityriasis lichenoides chronica. The patient has a dermatitis. Even today I tried to make a diagnosis of lichen planus, but the lesions on the volar surfaces of the forearms are distinctly not those of lichen planus. They are elevated papules, but the picture as a whole does not present the effect of a mosaic, each papule is discrete and separate. I thought of the possibility of lichen planus moniliformis for the eruption on the forearms, but with the other lesions on the body I could not establish that diagnosis. I do not believe this case is one of lichen planus.

**Creeping Eruption (Larva Migrans?)** Presented by DR E ALMORE GAUVAIN

R S, a youth aged 16, from the outpatient department of the Brooklyn Hospital, had several lesions on his right foot which were characterized by a red, elevated, tortuous ridge. There were no subjective symptoms. He had been living in Panama for several months, and the lesions developed soon after his return to the United States. Several of the lesions had been destroyed by ethyl chloride spray.

On presentation, he shows a large reddened area on the inner side of the left foot, where freezing with ethyl chloride had been done two weeks before. At the upper margin of this area is a red, tortuous ridge about 2 cm in length.

## DISCUSSION

DR C THOMAS CHIARAMONTE: There are too many recurrences after ethyl chloride freezing. I find that best results are obtained with electrocoagulation, electrodesiccation or the use of solid carbon dioxide. The region treated includes tissue slightly ahead of and slightly behind the visible advancing extremity of the lesion.

DR LESSER M FRUCHTBAUM: The lesions seen tonight are those due to a fungous infection.

## NEW YORK DERMATOLOGICAL SOCIETY

George C Andrews, M D, *President*

George M Lewis, M D, *Secretary*

Oct 23, 1945

**A Case for Diagnosis (Sarcoid?)** Presented by DR EUGENE F TRAUB

Dr G M B, aged 39, presented himself at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital about one week ago. He stated that he had had psoriasis, hay fever, asthma and sensitivity to iodides, acetylsalicylic acid, barbiturates and ephedrine. Locally, he was sensitive to tar, salicylic acid, sulfur and mercury.

His present eruption had first been noted three or four years before. It consisted of three nodular lesions scattered over the lower part of the abdomen, each varying in size according to the duration. The color was a deep purplish red. The peculiar feature of the eruption was the largest and oldest spot on the right side of the abdomen, which had a depressed center and a peculiarly rolled and elevated border. No such changes were seen in the other nodules. Two subcutaneous nodules were also felt in the left arm and on the right thigh.

The Wassermann reaction of the blood was negative. Histologic examination showed a chronic inflammatory nodule with necrosis, possibly tuberculosis cutis. The lesion was described as follows: "The section shows somewhat acanthotic epidermis with the corium filled with a sebaceous cyst, surrounded by inflammatory exudate containing giant cells of the foreign body type. Below this is an area of necrosis surrounded by a zone of chronic inflammatory cells and giant cells. The cellular exudate consists largely of connective tissue cells and round cells, as well as numerous plasma cells. There are occasional epithelioid cells, but not many."

## DISCUSSION

DR GERALD F MACHACEK, Long Island City, N Y: The histologic changes which were noted in sections of the biopsy specimen were not those of sarcoid. There was entirely too much necrosis. I consider the case to be one of a liquefying type of tuberculosis. Gumma should be considered as a possibility.

**Carotenemia in a Patient with Pernicious Anemia** Presented by DR MAURICE J COSTELLO

M H, a woman aged 58 (a private patient), consulted the presenter regarding puffiness of both lower eyelids which followed the softening of a paraffinoma on the bridge of the nose when she was exposed to the heat of a hair drier. At that time it was noticed that she had a yellowish discoloration of the palms, dorsal aspect of the fingers, wrists, elbows, soles, dorsal aspect of the feet, external malleoli, face, palpebral conjunctivas and soft palate.

During the past three years she has had about three hundred injections of liver extract for pernicious anemia. At present her diet is vegetarian, consisting of a large glass of celery and carrot juice, which she has been taking in addition to liver extract by mouth daily since May.

## DISCUSSION

DR MAURICE J COSTELLO Involvement of the mucous membranes to such a degree is unusual. The relation between the pernicious anemia and the carotenemia is interesting.

**Inflammatory Alopecia Marginalis** Presented by DR MAURICE J COSTELLO

M C H, a white woman aged 62 (a private patient), was first seen by the presenter two months ago. She stated that there has been profuse falling of her hair for the past three and one-half years. She thinks that the eruption followed her receiving an electric permanent wave. She has an unusual type of baldness. In addition to diffuse thinning of the hair of the scalp, there is a peculiar type of marginal inflammatory alopecia. A raised, red, indurated border, about  $\frac{3}{4}$  inch (0.5 cm) in width, separates the marginal bald areas from what remains of the hairy scalp. The areas of permanent baldness are atrophic and shiny and wrinkle easily.

The basal metabolic rate was normal. The Wassermann reaction of the blood was negative. The blood pressure was 165 systolic and 85 diastolic.

Treatments have consisted of administration of two subfractional doses of superficial roentgen rays to the five Kienbock-Adamson areas, ultraviolet irradiation and application of penicillin ointment, salicylic acid and sulfur ointment. She was given a prescription for "quinolor compound ointment" (10 per cent benzoylperoxide and 0.5 per cent "quinolor" [a mixture of 3 chlorine derivatives of 8-hydroxy-quinoline] in a base of equal parts of petrolatum and wool fat), which she was asked not to apply until after this meeting.

## DISCUSSION

DR MAURICE J COSTELLO In my experience this case is unique, for I have seen only 1 other case, that of a man who presented a similar, though much milder, dermatitis, which I presented before the Manhattan Dermatologic Society. In both instances the eruptions progressed in spite of therapy.

**Linear Lichen Planus** Presented by DR MAURICE J COSTELLO

W P, a man aged 33, had a thoracotomy on the right side, with removal of a piece of rib, in July 1942. Shortly thereafter another pocket of empyema appeared, and a part of another rib was removed on the same side. In January 1944 the first stage of a Khede operation was performed, and in May of that year the second stage was completed. Later the infection spread to the left lung, and the patient was transferred to St Joseph's Hospital for conservative therapy until the lesions of the left lung had absorbed. The bronchopleural fistula on the right side has continued to drain.

In December 1944 the patient first noticed a brownish, discolored, small cutaneous lesion at about the middle third of the right calf, and later similar lesions appeared on the dorsum of both hands and on the volar surface of both wrists, as well as on the penis. The lesion on the leg extended both proximally and

caudally, to form a continuous line at the present time. The other lesions have since partly disappeared.

## DISCUSSION

DR MAURICE J COSTELLO As Dr Andrews pointed out, there is no question as to the clinical diagnosis of linear lichen planus in this case. The individual lesions which make up the eruption are typical, and he has a sparse lichen planus eruption on the skin and the oral mucous membranes.

### Dermatitis Herpetiformis (Papular Type) Successfully Treated with Sulfapyridine Presented by DR MAURICE J COSTELLO

W M C, an elevator mechanic aged 59, was seen by the presenter for the first time on Sept 25, 1945. He stated that he had injured his ankle in January 1943. He was given ultraviolet radiation by another physician, which he claimed blistered his shin and caused a generalized pruritic eruption.

When first seen, he had a generalized eruption consisting of numerous severely excoriated papules. Several small vesicles were observed on the abdomen, where a hernia truss pad had rubbed against the skin. Sulfapyridine, 1 Gm three times a day, was prescribed. When he was seen a week later, the eruption had greatly improved, and the intake of sulfapyridine was reduced to 1 tablet of 0.5 Gm daily. On two occasions bullae were observed. Solution of potassium arsenite U S P in graduated doses was also administered because of intolerance to larger doses of sulfapyridine.

Because of an eczematized eruption on the dorsal aspect of his feet, he was given patch tests for sensitivity to the leather lining of his shoes and to the inner side of the tongue of his shoes. Both tests gave positive reactions in forty-eight hours, the shoe leather lining causing a bullous reaction. A few days later the patient had a severe exacerbation of his eruption, followed by the formation of several bullae the size of a dime to that of a half-dollar. Bullae formed under the adhesive tape which the patient had used to reinforce the patch test covers.

He states that he had known of his sensitivity to adhesive tape and leather dyes for some time, having had a bullous reaction to the former when adhesive tape had been applied after an operation and a similar reaction to leather boots when they were worn next to the skin to prevent injury to his legs, which his occupation frequently occasions. No eosinophils were observed in the bullae.

The following questions arise in connection with this case: 1. Did the reactions to the patch tests for leather and adhesive tape aggravate his dermatitis herpetiformis? 2. Was the solution of potassium arsenite the cause? 3. Has the patient become sensitized to sulfapyridine?

## DISCUSSION

DR GEORGE M LEWIS The favorable response of patients with dermatitis herpetiformis to treatment with sulfapyridine indicates that this substance may be used as a therapeutic test in doubtful cases. While there is little room for doubt that the results of treatment with sulfapyridine are better than those with other sulfonamide compounds, sulfadiazine and sulfathiazole have occasionally been effective.

DR MAURICE J COSTELLO I believe that this patient's eruption was aggravated by the patch tests for leather and adhesive tape to the extent that the eruption became severely pruritic and bullous.

NOTE—Since the patient's presentation before the society in October, the pruritic element has entirely disappeared. He now presents an occasional bullous lesion confined to the legs.

### Pityriasis Rubra Pilaris Presented by DR A BENSON CANNON

A W, a white woman aged 47, was admitted to the hospital one month ago complaining of a generalized eruption of four weeks' duration. She had had a laparotomy in March 1944 for an adenocarcinoma of the ovaries and tubes, followed

by high voltage roentgen therapy Three months ago she was again admitted to the hospital because of shortness of breath, at which time it was found that she had secondary adenocarcinoma of the lower lobe of the right lung and pelvic cellulitis The onset of the present rash was with a burning and tingling sensation of the toes and palms, with excessive perspiration A few days later her back and neck became itchy, at which time she noticed a red scaly eruption over those parts The rash has gradually spread over the entire face, neck, upper part of the chest and extremities There have been no subjective sensations since the onset of the itching

Examination reveals a fairly well developed and nourished, somewhat pale woman not acutely ill or uncomfortable The neck and face, the upper part of the chest and the scalp are uniformly covered with a macular, pale red eruption with fine desquamation Over the other parts of the skin, notably the lower part of the trunk and the thighs, were closely studded follicular, nutmeg-grater-like, slightly reddish papules the size of a large pinhead, giving the feel of goose flesh on stroking the parts The palms and soles and the palmar surfaces of the fingers were uniformly pale red, thickened and dry, with slight scaling along the borders of the hands Over the elbow region were thickened, finely scaly plaques 5 to 6 inches (12 to 15 cm) long by 3 inches (7.6 cm) wide

Laboratory analyses gave the following values serum phosphatase, 27 Bodansky units, urea nitrogen 6 mg and cholesterol 263 mg per hundred cubic centimeters, the cephalin flocculation test gave a negative result, the arsenic content was 0.015 mg per hundred grams of dry blood

A biopsy report established the diagnosis of pityriasis rubra pilaris

#### A Case for Diagnosis (Angiopericytoma?) Presented by DR GEORGE M MACKEE

U M, aged 12 years, has had an eruption on his back for four months It began with a single lesion which looked exactly like a pyogenic granuloma, it was so diagnosed and was destroyed by electrodesiccation, with the local use of procaine anesthesia Since then satellites have appeared in a circular area with a diameter of 7 cm The individual lesions range in diameter from 3 to 5 mm, with the same range of elevation The lesions are shiny, red and rather soft They look like angiomas A few of the larger lesions are exudative and crusted The histologic structure, while perhaps compatible with pyogenic granuloma, is much more suggestive of angiopericytoma This diagnosis is suggested also by the satellites There is no evidence of visceral involvement The tissue is embryonic and might respond to roentgen irradiation The inclination is to excise the entire area by means of plastic surgery

#### DISCUSSION

DR GEORGE M LEWIS It is my impression that the diagnosis is sarcoma because the lesion has developed so rapidly There are no other lesions on the body similar to this, and the appearance is atypical for molluscum contagiosum

DR FRED WISE The patient has been under my observation since his initial visit to the clinic I gained the impression that the papules surrounding the original lesion represent metastases of a primary, relatively benign form of sarcoma

SUBSEQUENT REPORT (DR GEORGE M MACKEE) The lesions in this case have disappeared as a result of two roentgen treatments, one month apart, consisting of 400 r at 120 kilovolts with a 1 mm aluminum filter

#### Trichoepithelioma Presented by DR GEORGE C ANDREWS

A S, a white woman aged 25, has had a growth on the right malar region for seven years Initially it was about the size of a pencil head, but recently it has begun to enlarge

Examination reveals an atrophic, depressed spot, irregularly circular and measuring about 2 cm in diameter, with scaling at the border With magnifica-

tion little pearl white papules and some telangiectases are visible throughout the area. There are many ridges, which are more or less regularly arranged throughout the lesion.

### A Case for Diagnosis (Sporotrichosis? Secondary Syphilis [Treated])

Presented by DR. GEORGE C. ANDREWS

G. V., a white woman aged 20, seven months ago had a generalized eruption which was diagnosed as secondary syphilis. The Wassermann reaction of the blood was positive. She had received four injections of oxyphenarsine hydrochloride intravenously, 2,000,000 units of penicillin intramuscularly and three injections of a bismuth preparation before being seen by the presenter, in May 1945 (five months ago). While she was in Florida, five months ago, a papule developed on the volar surface of the left wrist which she thought was an insect bite. About six weeks later she noticed tender swellings in the left epitrochlear area and in the left axilla. She had no chills or fever. The areas of tenderness enlarged and became more tender and the arm was painful to move.

Examination shows an erythematous papule, measuring 5 mm., on the volar surface of the left wrist. No central punctum could be noted. In the left epitrochlear area was a marble-sized, tender, firm node, with no erythema on its surface and no red streaks up the arm.

The swellings became more painful and enlarged. She received sulfadiazine, 0.5 Gm. four times a day for five days, without improvement. Two months ago she was given penicillin, 125,000 units intramuscularly, every three hours for five days, or a total dose of 5,000,000 units, without any effect. A new, indurated swelling developed just proximal to the epitrochlear node, the latter became fluctuant. About 15 cc. of thick, purulent material was obtained by aspiration. The papule on the left wrist was removed for histologic study.

For the past six weeks she has received roentgen radiation, 75 r weekly, through a 3 mm. aluminum filter, to each of three areas on the right arm and axilla. For the past month she has been taking 30 to 60 drops of a saturated solution of potassium iodide three times a day. The tenderness has subsided, but the masses have regressed only about 50 per cent of their volume.

The Wassermann reaction of the blood was 4 plus, the Wassermann reaction of the spinal fluid was negative, as were the reactions to the Frei and Ducrey tests. The intracutaneous test with old tuberculin was negative in a 1:100,000 dilution. Smears of pus stained for bacteria, fungi and acid-fast organisms were negative. Guinea pig inoculation gave negative results at the end of six weeks. Both aerobic and partially anaerobic cultures yielded no growth. Inoculation on Sabouraud's solid medium was negative for fungi. Agglutination tests of serum by the Board of Health gave negative results for tularemia, brucellosis, typhus and typhoid.

The total white blood cell and differential counts were 11,500 on August 21 and 16,500 on August 27, with 84 per cent polymorphonuclear neutrophils.

The histologic report of the papule on the left wrist was that of "chronic inflammatory tissue." The urine was normal.

### DISCUSSION

DR. GEORGE M. LEWIS: It would seem that sporotrichosis could be ruled out by cultural methods, since *Sporotrichum schenckii* is one of the easiest fungi to grow on artificial mediums. The cutaneous test is also highly specific. If this fungous disease can be eliminated from consideration, I suggest that inoculation tuberculosis be considered as a strong possibility.

### Epidermodysplasia Verruciformis. Presented by DR. FRANK C. COMBES

L. J., a girl aged 15, after an attack of measles at the age of 5, had the onset of a dermatosis, which has remained practically unchanged in appearance and

distribution There is no history of familial consanguinity, and she has a younger sister

Examination discloses the presence of hundreds of verrucous papules situated on the backs and palms of the hands, the soles, wrists, thighs, forehead and chin and along the hair line of the scalp anteriorly The smallest papules measure 1 to 2 mm in diameter and are rounded or polygonal, with truncated borders and a smooth, mammulated surface The color varies from reddish to brownish violet On some lesions grayish scale can be detected There are no subjective symptoms except for slight pruritus in warm weather

#### **Glossitis Rhomboidea Mediana** Presented by DR RAY H RULISON

Mr J H, aged 26, married and the father of a healthy 3 year old child, states that about three and one-half months ago he suddenly became aware of a somewhat painful sensation in his tongue The pain is no longer present Some discomfort is noticed on eating, but otherwise the patient is not inconvenienced He was discharged from the Army this spring for a disability There is no history of venereal disease

Examination shows a longitudinal area of glossitis, about 1 inch (25 cm) long and  $\frac{3}{16}$  inch (48 mm) wide, in the center of the tongue, with a slightly denuded area in the center

The Wassermann reaction of the blood was negative No other tests were made

The patient has been given a mixed vitamin preparation in fairly large doses, without any change in the appearance of the eruption

#### DISCUSSION

DR RAY H RULISON I agree that the lesion is situated farther forward on the tongue than in the cases previously described and published

#### **Larva Migrans** Presented by DR EUGENE F TRAUB

H B, a man aged 41, states that about three or four weeks prior to the presentation he had spent a few hours at Miami Beach and the following day he noticed severe itching on the center of the left palm, which by the next day had developed into a small red spot In the course of a few days there was an area on the left elbow and others on the right buttock and the right shoulder

He received various local remedies, without benefit The track of the larva had been thoroughly cauterized with an electrosurgical knife, leaving a deep groove and some scarring, but without arresting the eruption

The patient has now received one treatment with ethyl chloride spray, and a number of the areas appear quiescent

### SAN FRANCISCO DERMATOLOGICAL SOCIETY

Otto E L Schmidt, M D, *Chairman*

Frances M Keddle, M D, *Secretary-Treasurer*

Oct 26, 1945

#### **Epidermolysis Bullosa** Presented by DR NORMAN N EPSTEIN

A A B, a  $7\frac{1}{2}$  year old Mexican boy, was first presented before the American Dermatological Association in June 1938 (Epidermolysis Bullosa, ARCH DERMAT & SYPH 39 1052 [June] 1939) His general condition at birth was good, but physical examination one hour later revealed clubfeet and circumscribed, sharply defined, depressed, smooth, reddened areas on the ankles and feet A bulla, 1 cm in diameter, was present on the dorsum of the left index finger Buccal lesions were also present

Gradual improvement occurred, but one year later more bullae spontaneously appeared at the pressure sites and on the abdomen, mouth and penis. The course up to the present has been one of recurrent formation of vesicles and bullae, involving at various times most of the extensor surfaces and the buccal mucosa. The lesions heal with some scarring and pigmentation.

Treatment has emphasized the prevention of trauma and secondary infection. The topical medicaments employed have included various shake lotions, wet dressings, gentian violet medicinal, various ointments and hydrogen peroxide mouth washes. One per cent ammoniated mercury ointment U S P has proved most beneficial. A course of injections of estrogenic substances was given, without noticeable effect. This patient has 2 sisters, aged 6 and 8 years, who are in good health. He has 1 brother, aged 4 years, who has a similar but more benign form of the disease.

#### **Epidermolysis Bullosa (Acquired)** Presented by DR ORLAND F MONTGOMERY

About one year ago, E. D., a white man, noticed that the skin on the backs of the hands came off with slight trauma. This condition has grown progressively worse, until now the slightest bump will remove irregular, fingernail-sized pieces.

For the past several months various-sized bullae have been present at all times on the dorsa of the fingers of both hands. Particular attention is called to the milium-like bodies on the dorsa of the hands.

There is no history of a similar disease in the family. Irregular pigmentation follows the healing of all lesions and does not disappear.

The patient has a mild intertriginous dermatophytosis of the feet.

#### DISCUSSION OF CASES OF DR EPSTEIN AND DR MONTGOMERY

DR HIRSH E. MILLER. I do not believe that there is any question about the diagnosis of the disease in these 2 youngsters. They have epidermolysis bullosa of the hereditary type. There may be some question in regard to the diagnosis of the man's lesions. Sometimes it is difficult to be positive about the diagnosis of the acquired type of epidermolysis bullosa early in the course of the disease.

I recall a man with the acquired form of the disease whom I had under observation a few years ago. He worked as a laborer in an ink factory in Berkeley. He had a half-dozen bullae or more on the backs of his hands, many of them as large as a pigeon egg. They were present on the knuckles and the parts of the hands most exposed to injury. It was of interest that these bullae did not rupture for several weeks despite the fact that he continued his work as a laborer.

The lesions on the hands of the man presented tonight are small, they are present on the backs of the hands but not on the knuckles, and all are ruptured. He states that this is because he punctures the bullae and aspirates the liquid. There is no scarring. This may be the acquired type of epidermolysis bullosa, but I am not certain of it.

DR REES B. REES. In the recent literature the subject of epidermolysis bullosa has been discussed in connection with military life because of its disabling feature in soldiers on whose feet the lesions develop.

DR ORLAND F. MONTGOMERY. It is unfortunate that the large bullous lesions which were on this patient's hands when I first saw him are not present tonight. There were some as large as a finger nail at that time.

Of particular interest is the fact that most of the bullae occur on the dorsa of the fingers and that the traumatic excoriations are on the backs of the hands.

SUBSEQUENT REPORT (Dr Orland F. Montgomery).—Since this meeting the patient has received eight biweekly intramuscular injections of chorionic gonadotropin. Since the first week of treatment there have been no new bullae, but the skin remains fragile and slight trauma produces irregular excoriations. I have tried, with small success, to toughen the skin with aluminum salts and oxidizing agents, such as potassium permanganate.

**Bullous Dyskeratosis (Familial Benign Chronic Pemphigus)** Presented by DR HIRAM E MILLER and DR REES B REES

A F a white man aged 35, was originally seen by the presenter three years ago, while he was working for the Western Pacific Railroad. No record of that visit is available. He was seen subsequently on July 23, 1945, at which time he was found to have an eruption on the neck and the left side of the scrotum, which had appeared in 1938. He stated that he had received several roentgen treatments, without benefit. The application of silver nitrates to the lesions had proved ineffective. The individual lesions which we found on examination were grouped, vesicular, polycyclic and reminiscent of dermatitis herpetiformis. A dollar-sized, exudative, eczematous plaque was present on the left side of the scrotum. Biopsy of a specimen taken from a vesicular lesion on the left side of the upper part of his back presented dyskeratosis and other changes reminiscent of Darier's disease (keratosis follicularis), including formation of clefts. The size of the clefts was compatible with that of lesions in dermatitis herpetiformis or pemphigus, but the changes were not typical of either disease. A course of arsenic therapy in the form of a preparation containing arsenic trioxide (Asiatic pill),  $\frac{1}{9}$  grain (7 mg) to be taken morning and night for twenty-five days, was prescribed. Solution of aluminum acetate N F was advised for tropical use in a 1:15 dilution.

When he was seen on Sept 12, 1945, he stated that the lesions on the chest began to clear within a few days after he commenced taking the preparation of arsenic. The entire eruption was much improved. At that time he was observed to have irregular, scurfy and scaly, dusky reddish patches, especially on the posterior aspect of the sides of his neck, which appeared ecthymatous with the presence of flaccid, purulent blisters. The patch of fissured and exudative eczema on the scrotum remained the same. The patient stated that his father has had a similar eruption (for thirty years, beginning as "barber's itch" on the face and coming out later on the neck as blisters). One brother and 2 sisters have had no cutaneous disturbances. At the time of the second visit vitamin A was prescribed, in a dose of 100,000 U S P units daily.

The eruption on his neck has cleared since the time we saw him last.

His father is presented also.

#### DISCUSSION

DR HARRY J TEMPLETON, Oakland, Calif. The histologic picture is classic and could be substituted for one of the illustrations in the original description of the disease. The lesion on the scrotum I think is not typical and could be called simply *eczema en plaque*. It would be interesting to do a biopsy, as it would be easy to get the entire area for microscopic examination. The patient would permit this.

DR REES B REES. The history reveals an additional point of interest regarding the lesions which are no longer active on the neck. The patient states that the eruption has cleared on two occasions in the past. The disturbance began in 1938. It tends to clear in the fall and recurs in the spring. The father has a history of a similar eruption on the neck. The father is 66, and the disturbance began fifteen or twenty years ago. Hailey and Hailey (Familial Benign Chronic Pemphigus, ARCH DERMAT & SYPH **39** 679 [April] 1939) and Ayers and Anderson (Recurrent Herpetiform Dermatitis Repens, *ibid* **40** 402 [Sept.] 1939) originally described this disease in the same year. The former authors reported 4 cases, in 1 of which there were lesions in the groin, as well as elsewhere. The latter authors described 5 cases, 2 of the patients being women and 3 men. All 3 men had scrotal lesions or perineal lesions as well.

As Dr Templeton mentioned, the histologic changes in the case presented tonight are characteristic.

**Keratosis Follicularis (Darier's Disease)** Presented by DR FRANCES M KEDDIE

B W, a man aged 28, has had an eruption on the back, face and extensor surfaces of the shoulders for the past fifteen years. He states that his father and

2 of his 2 sisters have similar eruptions. The eruption began on the lumbar region and on the extensor surfaces of the arms. During the past five years the patient has been in the submarine service, where the temperature of the engine room is frequently 140 F. The eruption has gradually spread up the back and appeared on the face. The chest shows lesions in areas that one year ago were burned with hot coffee. The eruption shows follicular scaling on a confluent reddish base.

## DISCUSSION

DR OTTO E. L. SCHMIDT: Has any therapy been given this patient?

DR FRANCES M. KEDDIE: The patient stated the belief that exposure to the high temperatures of the engine room for a period of five years caused the spread of his disease. He has had no previous therapy.

### A Case for Diagnosis (Papular Urticaria? Dermatitis Herpetiformis?)

Presented by DR HARRY J. TEMPLETON, Oakland, Calif

L. S., a white man, consulted the presenter on Jan 26, 1945, because of a pruritic papular eruption on the covered portions of the body, of two months' duration. He is a painter and had felt that his occupation had something to do with it. However, the exposed areas are normal.

The diagnoses originally considered were papular urticaria, insect bites and folliculitis. Even dermatitis herpetiformis was considered at one time.

Elimination diets have failed to help him. Physical examination by his physician failed to disclose any illness or focus of infection. Examination of the blood and urine gave normal results. There was no apparent relation to ingestion of drugs.

No fleas or mosquitoes were present in his environment. During one month at Lake Tahoe the eruption did not disappear.

Empiric therapy, namely, "hapamine" (a chemical combination of histamine and despecciated horse serum globulin), lobeline and staphylococcus ambotoxoid, by injection, and hydrochloric acid and histaminase, by mouth, has been of little value.

## DISCUSSION

DR MERLIN T. R. MAYNARD, San Jose, Calif: I am inclined to diagnose this eruption as dermatitis herpetiformis complicated by folliculitis. The lesions over the scapulas and the distribution on the arms would be sufficient to sustain this diagnosis. Physical examination should be made, and the diagnosis should be confirmed by further laboratory examinations.

DR JAMES W. BAGBY, St. Louis\* (by invitation): The case impresses me as one of dermatitis herpetiformis because of the grouping of the lesions, the distribution, the tendency to pigmentation in healed areas and the fact that the itching stops when the vesicles are broken. I believe a trial with sulfapyridine would prove diagnostic.

DR HARRY J. TEMPLETON, Oakland, Calif: All sorts of possibilities have been considered. He was given elimination diets, with no improvement. General physical examination for focal infection showed no deviation from normal. Results of analyses were normal. I thought a change of environment might be of benefit and sent him to Lake Tahoe for a month. Insects, particularly fleas, both from cats and dogs, were considered in the diagnosis and it was suggested to him that he spray his home with insecticides.

I have thought of the possibility of dermatitis herpetiformis. Certainly, the eruption is not typical, and the case is not a good one to present. The patient simply itches and scratches. One does not see anything. I have thought of using an arsenic preparation or sulfapyridine.

\* At the time of this meeting Dr. Bagby was serving as a commander in the United States Naval Reserve.

DR JOHN M GRAVES I suggest the use of sulfadiazine, which is much less toxic than sulfapyridine. It is effective with some patients.

DR HIRAM E MILLER I suggest the use of sulfapyridine. In cases of dermatitis herpetiformis in which I have used sulfapyridine for a few months with success and then changed to sulfadiazine the lesions have promptly recurred. Admittedly, sulfapyridine is more toxic than sulfadiazine, but it is certainly more efficient in the treatment of this disease.

DR MERLIN T R MAYNARD, San Jose, Calif I understand that sulfapyridine has been used in rather small doses. I should like to know what dose Dr. Miller is using.

DR HIRAM E MILLER I usually start with 1 Gm of sulfapyridine four times a day, given at 8 a. m., 12 noon, 4 p. m. and 8 p. m., and then reduce the dose to 0.5 Gm four times a day.

#### Multiple Keloids Presented by DR JOHN M GRAVES

J. R., a Negro aged 42, was first seen in the University of California dermatologic clinic on Oct. 23, 1945. Since he was 8 or 9 years old, firm, irregularly shaped elevations of the skin have developed spontaneously and after any injury. The growths have spread progressively, new ones appearing from time to time, eventually to join the older lesions in covering a large portion of the chest and shoulders. The initial tumor was in the sternal region.

At present there are firm, elevated, irregularly shaped and hypesthetic pads, with overhanging edges involving the anterior and posterior aspects of the trunk, shoulders and arms. The overlying epidermis is smooth, thin and glossy. An occasional small ulcerated area is encountered.

#### DISCUSSION

DR ERVIN EPSTEIN, Oakland, Calif It is of interest that the keloids in this case are familial, occurring only on the male side of the family. The patient's uncle, father and grandfather have keloids, but no member of the female side of the family has been so affected.

DR ORLAND F MONTGOMERY Apparently, some dark-colored people of the South Pacific are able to produce keloids at will.

I recall in a long past issue of the *National Geographic Magazine* pictures of Solomon Islanders on whose backs linear excoriations had been made and the juice of the mangrove rubbed into them. It was stated that large keloids in geometric patterns almost always follow this procedure.

DR MERLIN T R MAYNARD, San Jose, Calif Considering the tribal custom of intermarriage among these native tribes and their use of irritants to produce keloids, it is apparent that a familial tendency in these tribal cases may develop.

DR STUART WAY May I comment on the treatment of keloids? Until two years ago I had always used roentgen rays or radium. Since then I have obtained equally good results by applying solid carbon dioxide at intervals of several weeks. Usually six applications are sufficient. Telangiectasia should not develop when this method is used.

#### Leiomyoma Cutis Presented by DR GRANT MORROW (by invitation)

J. D., a man aged 48, presents cutaneous lesions on the back and shoulders. They started on the back and have increased in size and number during the past twenty years. The largest tumors are painful when the body is exposed to cold or when the patient is emotionally upset.

The lesions are elevated, firm nodules of various sizes, ranging from 2 to 10 mm. The largest lesions are on the back. All are oval or elliptic and of normal color or light brown. There is no lymphadenopathy. Physical examination showed nothing unusual. The serologic test for syphilis was negative.

Biopsy showed smooth muscle fibers running in many directions.

## DISCUSSION

DR M G BUTLER (by invitation) This is a classic picture of leiomyoma cutis, a type that Dr F Weidman is especially interested in I have nothing further to add

DR HARRY J TEMPLETON, Oakland, Calif Years ago Dr Miller pointed out the typical rubbery "feel" of these lesions

**Rhinoscleroma** Presented by DR F G NOVY JR, Oakland, Calif

T P J, a Central American man aged 37, was first seen in the University of California otorhinolaryngologic clinic in May 1933 At that time both nares were filled with exuberant granulation tissue and a diagnosis of rhinoscleroma was made, which was confirmed by histologic examination in June 1933 and again in December 1934 There has been subsequent involvement of the hard and soft palate the upper alveolar ridge, the left nasolabial fold and the right external auditory canal

To date the patient has received four courses of roentgen therapy (2,200, 2,000, 1,200 and 1,000 r, respectively) The last course of treatment was completed on Aug 6, 1945

This patient was presented at a meeting of the San Francisco Dermatological Society on Dec 4, 1936 (ARCH DERMAT & SYPH 36 1241 [Dec] 1937), again by Dr John M Graves at the combined meeting of the Los Angeles and the San Francisco Dermatological Society on Feb 12, 1938 (ibid 38 494 [Sept] 1938) and again by Dr F G Novy Jr before the San Francisco Dermatological Society on June 8, 1938 (ibid 39 1058 [June] 1939)

## DISCUSSION

DR MERLIN T R MAYNARD, San Jose, Calif Dr Esteban Rayes of San Salvador, who has seen many cases of this kind there, stated that practically all cases occurred in camps where the bark is processed from which a certain red dye is produced Flies found there in large numbers were thought to be the vector of the disease

DR HIRAM E MILLER This patient has been of particular interest to me because it is the first case of rhinoscleroma that I have been able to follow from early in the course of the disease Ordinarily, one sees the patient at the end of the disease

Dr Weidman did not accept the diagnosis of rhinoscleroma when this patient was presented at a meeting of the American Dermatological Association a number of years ago I feel certain that he would agree with the diagnosis now

**A Case for Diagnosis (Mycetoma [Maduromycosis]?)** Presented by DR HIRAM E MILLER

S C a white man aged 35, was first seen in the University of California dermatologic clinic on Dec 4, 1941, with a history of firm, tender subcutaneous nodules developing over the midplantar surface and lateral aspect of the left foot for the past two years At intervals one or more of the lesions softens and ruptures spontaneously, discharging a thick pus

The patient was born in Mexico but moved to California at the age of 14 He worked on a ranch in Fresno for two years and then came to San Francisco, where he has resided ever since He gives no history of injury or of previous illness Two sisters are said to have died of tuberculosis

The results of histologic examination (Dec 11, 1944) were not diagnostic but were considered compatible with multiple idiopathic hemorrhagic sarcoma (Kaposi)

The reactions to tuberculin (1 100,000) and coccidioidin were negative, as was the coccidioidin complement fixation and precipitin reactions The Wassermann reaction of the blood was negative on two occasions Cultures of material

from the lesions showed no growth on two occasions. Roentgenograms of the left foot revealed no evidence of bony involvement.

Treatment has consisted of oral administration of solution of potassium arsenite U S P, seven injections of oxophenarsine hydrochloride ("mapharsen"), 0.06 Gm., and hot soaks. Progressive improvement has occurred since discontinuing oxophenarsine hydrochloride in June 1945.

NOTE—A biopsy specimen subsequently was taken from a small subcutaneous abscess on the upper surface of the foot. Characteristic chalk-colored granules were obtained, which under the microscope established a diagnosis of mycetoma (maduromycosis).

#### DISCUSSION

DR HARRY J. TEMPLETON, Oakland, Calif. It seems to me that one must consider mycetoma, since the patient comes from a country next the tropics, Mexico. He has tumefaction of the sole and dorsum of the foot with healed and open sinus tracts. He states that pus has exuded from these sinus tracts. Although no fungus has yet been found, mycetoma would be my working diagnosis.

DR ERVIN EPSTEIN, Oakland, Calif. I think that the lesions of the skin in this patient are consistent with the diagnosis of multiple idiopathic hemorrhagic sarcoma. The amount of swelling that this man has also goes with that disease. However, usually there is more cutaneous change before subcutaneous involvement.

DR L. H. WINER, Beverly Hills, Calif. (by invitation.) These lesions clinically are subcutaneous infiltrated nodules which seem to form strands or cords on the soles and dorsa of the feet. There was also a deeper subcutaneous globular lesion which was very slightly elevated. From the clinical picture I could not make any diagnosis. Histologic section showed formation of new blood vessels, frank hemorrhage into the connective tissue and proliferating connective tissue. I could well agree with the diagnosis of multiple idiopathic hemorrhagic sarcoma (Kaposi).

DR HIRAM E. MILLER. A diagnosis has not been made in this case. I do not believe that he has either Kaposi's hemorrhagic sarcoma or mycetoma.

Multiple idiopathic hemorrhagic sarcoma generally occurs in persons well over 40 years of age. The patient is 35. The disease is generally bilateral. In this man it is unilateral. The infiltrated plaques usually observed are not present. The histologic changes were not diagnostic but perhaps were compatible with a diagnosis of hemorrhagic sarcoma.

Mycetoma is uncommon in Northern California but is frequently seen in Mexico. This man was born in Mexico but has lived in California for twenty-one years. A few discharging sinuses were present when he was first examined, but no sulfur granules were found. The sinuses healed while he was being given oxophenarsine and have remained so since that time. It is difficult for me to believe that a mycetoma would behave in this manner.

The disease may be an anomaly of the peripheral vessels in the foot. Investigation of this case will be continued.

DR ORLAND F. MONTGOMERY. Did the patient have any roentgenograms?

DR HIRAM E. MILLER. Roentgenograms were taken of the foot several months ago, and there was no evidence of bony involvement.

**A Case for Diagnosis (Sarcoid? Basal Cell Epithelioma?)** Presented by  
DR ORLAND F. MONTGOMERY

A W., a man aged 47, one month ago had a small red "pimple" on his nose. It bled when his wife opened it. The lesion has grown larger and is symptomless.

Examination reveals above the ala of the right side of the nose a round, lima-bean-sized, dome-shaped tumor of firm consistency but with a suggestion of fluctuation in its center. Several telangiectases course over the tumor's edge.

On two occasions the mass has been opened, without pus or sebaceous material being found.

## DISCUSSION

DR ORLAND F MONTGOMERY When I first saw the patient, I had not the slightest idea what was wrong with him, nor do I know now I considered sarcoid, basal cell epithelioma or a localized pyodermic lesion, so often seen preceding or accompanying acne keloid

DR MERLIN T R MAYNARD, San Jose, Calif I should call it simply a sarcoma, not a sarcoid I have seen two similar lesions in the past, one in a baby a few months old and another on a cheek of a man Both were perfectly circular, as this one is, soft to the touch and pseudofluctuant The only method of treatment is excision of the whole growth, followed with irradiation Frozen sections should be made at the time of operation Plastic repair could be done later It is clear in my mind that this lesion is a sarcoma

DR HIRAM E MILLER I see no reason that a biopsy should not be performed, a diagnosis established in twenty-four hours and treatment then begun

DR ORLAND F MONTGOMERY It is obvious that a biopsy should be made However, I am extremely reluctant to carve up the face when it can be avoided Too many biopsy specimens are taken from the face just to satisfy curiosity

SUBSEQUENT REPORT (Dr Orland Montgomery) —After the meeting it occurred to me that this lesion might be the Brocq-Pautrier angiolupoid, which occurs usually on the side of the nose or near the inner canthus of the eye

Biopsy material was obtained There was complete disagreement in diagnosis by local pathologists

The section was sent to Dr Hamilton Montgomery, who reported as follows "The section is strongly suggestive of lymphoblastoma without being specific as to type The lesion could be a lymphocytoma or lymphatic leukemia It did not look like lymphosarcoma or mycosis fungoides"

### Lymphoblastoma? Presented by DR FRANCES TORREY

E L, a white man aged 55, has had a generalized eruption for about twenty years

At present he has a generalized erythroderma with lichenification and scaling over the entire body, accompanied with considerable pruritus There are several indurated, painful ulcerations, each 2 to 4 cm in diameter, on the thighs and trunk These have been present for about one year There is a generalized adenopathy The leukocyte count on Sept 14, 1945 was 12,800 and the erythrocyte count 4,550,000, per cubic millimeter There were 9 per cent eosinophils

The histologic structure of the generalized eruption showed only a chronic inflammatory reaction Biopsy of a specimen from one of the ulcerated areas on the thigh showed chronic inflammation of the skin with ulceration

During the last twenty years, the patient has been seen by various dermatologists, including Drs Sutton, O'Leary and Hamilton Montgomery The diagnoses have included parapsoriasis, psoriasis and mycosis fungoides

This patient was seen at the Radiation Laboratories in Berkeley on October 9 At that time an injection of radioactive phosphorus, 765 microcuries, was given

The department of roentgenology has begun treatment with the following technic Irradiation of the entire body with a voltage of 200 kilovolts, approximately 20 r being given at each dose

## DISCUSSION

DR L H WINER, Beverly Hills, Calif (by invitation) This case brings up the perennial debate frequently encountered in dermatologic societies "Is parapsoriasis the same as mycosis fungoides, or does parapsoriasis change into mycosis fungoides, or are the two diseases different, distinct clinically as well as histologically?" I could not diagnose this eruption as parapsoriasis from the histologic sections because the epidermis is acanthotic, whereas in parapsoriasis the epidermis becomes thin with degeneration of the basal cells Here the basal cells are normal

There is definite infiltration or proliferation in the uppermost cutis, and to a slighter degree in the lower cutis. I favor the diagnosis of a proliferation, because relatively more nuclei are present than cellular cytoplasmic elements. Whether these cells are infiltrating or proliferative is debatable. I think the lesion is a lymphoblastoma or the premycotic mycosis fungoides. The pathologic change is in the reticulum of the connective tissue. The reason these nests of cells are seen in the cutis is that the reticulum is abundant throughout the cutis.

DR M G BUTLER (by invitation) I believe this case is one of mycosis fungoides, it is no longer premycotic.

DR MERLIN T R MAYNARD, San Jose, Calif I should like to see a section from one of the active areas. It must not be forgotten that typical psoriasis may go on for years and the lesions subsequently exfoliate and become typical lymphoblastoma. In this instance I incline to the diagnosis of psoriasis of exfoliative form rather than a lymphoblastoma.

DR HIRAM E MILLER I agree with Dr Butler. The diagnosis is lymphoblastoma perhaps mycosis fungoides, but not the prestige of anything.

DR FRANCES T TORREY This man has been followed for many years by numerous dermatologists. Various diagnoses have been made. A biopsy specimen was taken from one of the ulcerated lesions and from the generalized eruption. Neither showed histologic changes characteristic of lymphoblastoma. However, clinically the generalized eruption and the areas of ulceration are more suggestive to me of lymphoblastoma. A lymph node is to be removed for examination.

#### A Case for Diagnosis (Spiegler-Fendt Sarcoid? Lupus Erythematosus?)

Presented by DR HARRY J TEMPLETON, Oakland, Calif

F S M, a white man aged 70, consulted the presenter on Sept 25, 1945, because of a sharply margined, pinkish, velvety plaque to the right of the nose, measuring about 3 by 4 cm. It had been present about eight months and had been treated with roentgen rays by other physicians, without benefit.

The Kahn reaction of the blood was negative. The erythrocyte count was normal, the leukocytes numbered 7,850, with 3 per cent large lymphocytes, 28 per cent small lymphocytes, 5 per cent monocytes, 64 per cent neutrophils (1 per cent juvenile forms, 7 per cent stab forms and 56 per cent segmented forms), no basophils and no eosinophils.

The histologic examination was reported by Dr Gertrude Moore, as follows:

"Microscopic examination shows skin in which there are closely spaced hair follicles and sebaceous and sudoriferous glands. Throughout the tissue, but most abundant in the midcutis, adult lymphocytes are observed in dense aggregates, without follicular structure. They are also seen in collars around blood vessels and the cutaneous appendages and as a diffuse infiltration extending up into the papillae. Associated with the lymphocytes is an occasional plasma cell. There is pronounced edema of the connective tissue, and the squamous epithelial covering is stretched and thin. Blood vessels are present in normal number and distribution.

"*Comment*—There are certain differences between this histologic picture and that described for the Spiegler-Fendt sarcoid. In the present lesion there are no reticulum cells or multinucleated giant cells, the larger aggregates of lymphocytes do not have a follicular structure, and blood vessels show no evidence of proliferation.

"The histologic picture is quite compatible with the infiltrations seen in chronic lymphatic leukemia, but such an entity may be ruled out by studies of the blood and biopsy of bone marrow. The mature appearance of the lymphocytes and the absence of mitoses and tumor-like nodules make lymphosarcoma extremely unlikely. There is none of the histologic characteristics of Hodgkin's lymphoblastoma. A final conclusion cannot be drawn from the histologic studies, but in general it may be said that the picture is not that of neoplastic disease but, rather, one of an inflammatory process."

Morphologically, the diagnosis seems to rest between Spiegler-Fendt sarcoid, lymphoblastoma and lupus erythematosus

## DISCUSSION

DR L. H. WINER, Beverly Hills, Calif (by invitation) I favor the diagnosis of lupus erythematosus from the histologic point of view because of the hyperkeratotic follicular plugging, epithelial atrophy and discrete islands of lymphocytic infiltration, characteristics which are not those of Spiegler-Fendt sarcoid. Dr S. E. Sweitzer described one of the first cases in this country (*Sarcomatosis of Spiegler*, *ARCH DERMAT & SYPH* **11** 481 [April] 1925), which terminated fatally as a case of lymphosarcoma. Therefore I consider Spiegler-Fendt sarcoid as lymphosarcoma.

DR OTTO E. L. SCHMIDT Certainly the clinical picture is not clearcut.

DR HARRY J. TEMPLETON I think that only time will tell whether the lesion is lupus erythematosus profundus or Spiegler-Fendt sarcoid. When I first saw the patient there was no scaling at all. In favor of Spiegler-Fendt sarcoid, morphologically, were the sharply elevated, velvety plaques without, at that time at least, any scaling. Histologically, either diagnosis could be defended. The round cells are numerous and large for the round cells of lupus erythematosus, which are usually remarkably small. Against Spiegler-Fendt sarcoid is the fact that the patient has not responded to roentgen radiation given by other physicians. During the last week he has been taking an arsenic preparation by mouth, and since that time the lesions have become scaly. If he does not respond to arsenic therapy in a month, as Spiegler-Fendt sarcoid is supposed to do in a high percentage of cases, I may change to gold sodium thiosulfate and solid carbon dioxide.

#### A Case for Diagnosis (Idiopathic Atrophy of the Skin) Presented by DR H. V. ALLINGTON, Oakland, Calif

O. H. D., a white man aged 21, is presented with oval, pigmented, atrophic areas of skin which have been developing gradually during the past three years. The largest and oldest lesions are on his flanks and the lateral surfaces of his hips. Newer lesions are also present on the extremities. In the involved areas the skin is obviously thinned and the veins are easily visible through it, but it has not lost its elasticity completely. It shows grayish pigmentation. There is no surrounding redness or infiltration, and there has been none throughout the course of the disease. The lesions develop insidiously, being first evidenced as increased pigmentation. They are asymptomatic, and sensibility to touch, pain, heat and cold is not impaired.

He had the usual childhood diseases and, in addition, had diphtheria in childhood. He had scarlet fever about one year ago. An appendectomy was performed in 1936.

The results of physical examination were otherwise essentially normal. Examination of the nose and throat showed no disease. The ulnar nerves were not enlarged or nodular. The Kahn reaction of the blood was negative.

Microscopic sections of involved skin showed thinning and increased pigmentation of the epidermis. There was atrophy of the sebaceous and sweat glands. The hair follicles appeared normal. The corium showed clumping and fragmentation of the collagen, which took the eosin stain deeply. The small amount of subcutaneous tissue included in the section appeared normal.

## DISCUSSION

DR H. V. ALLINGTON, Oakland, Calif I first saw this patient at the time he was hospitalized for an attack of acute gastroenteritis. The cutaneous lesions were an incidental finding. I have no other diagnosis to offer than idiopathic atrophy. From the clinical appearance I thought that the subcutaneous fat would be completely lost, but the sections show a bit of normal-looking subcutaneous tissue with fat adherent to it. There is no history or present appearance of infiltration or erythema around the margins to suggest scleroderma.

DR L. H. WINER, Beverly Hills, Calif (by invitation) I agree with the diagnosis because the skin shows increase in pigmentation. Microscopically, the epi-

dermis is of normal thickness, no atrophy is present. In idiopathic atrophy there is atrophy. Here the rete pegs seem normal in their outline, and there is no tendency to flattening out, such as one sees in scleroderma. In the papillary bodies there are cells full of pigment chromatophores. The only possibility other than early atrophy is a fixed drug eruption. At the time he had the gastroenteritis he was probably given a bismuth compound, which became implanted in this particular area of skin that we have seen.

DR JAMES W. BAGBY, St. Louis (by invitation). I asked the patient whether there had been episodes when the lesions became red and swollen and itched. He said there had not, a fact which would be against the diagnosis of a fixed drug eruption.

DR H. V. ALLINGTON, Oakland, Calif. The episode of gastroenteritis occurred within the last year, whereas the present cutaneous lesions began appearing over three years ago.

### Cutaneous Torulosis in a Patient with Hodgkin's Disease Presented by DR FRANCES A. TORREY

This case was previously presented by Dr. Torrey at the meeting of the San Francisco Dermatological Society, April 20, 1945.

W. R. H., a white man aged 42, was treated in the University of California dermatologic clinic from May until September 1935 for a seborrheic eczema involving the scalp, face and body. At that time the eruption was said to have been present for twelve years and to have had a variety of treatments by a number of dermatologists.

On March 13, 1945, he was referred to the University of California Visible Tumor Clinic by Dr. Oaks, whom he had consulted on March 5 because of an ulceration on the back of his neck. The lesion had been present about four months and was 2.5 cm. in diameter. Dr. Oaks excised the ulcer together with a wide margin of the skin and removed the underlying cervical nodes. The histologic examination of the ulcer showed a squamous cell epithelioma. There was no evidence of metastasis of the epithelioma into the cervical nodes. However, on the basis of the nodes examined a diagnosis of Hodgkin's disease was made. At that time there was a generalized adenopathy with large firm nodes palpable in both axillae. Biopsy of one of these nodes confirmed the diagnosis of Hodgkin's disease. Biopsy of tissue from one of the chronic lesions on the skin of the back on April 4 showed only chronic inflammation.

There is a massive formation of verrucae acuminatae over the entire genital and anal areas, and verrucae are also present on the dorsa of the hands and arms.

Examination of the blood on April 12 showed 88 per cent hemoglobin, 4,400,000 erythrocytes and 22,250 leukocytes with 60 per cent filamentous forms, 29 per cent nonfilamentous forms, 4 per cent eosinophils, 2 per cent small lymphocytes and 5 per cent monocytes. The Kahn reaction of the blood was negative.

On July 24 the patient returned with a crusted lesion, 1 cm. in size, on the midposterior aspect of the neck, clinically suggestive of a basal cell epithelioma. A biopsy was performed and the lesion treated by curettage and desiccation. The histologic report at that time was "epithelial hyperplasia with secondary infection."

On October 11, when the patient was again seen, an epitheliomatous-appearing lesion, 2 cm. in size, was present at the same site, and he was referred to the surgical clinic for its excision. In sections of this specimen members of the department of pathology discovered numerous small, round, double-contoured bodies, morphologically similar to *Cryptococcus neoformans* (*Torula histolytica*). Budding forms were infrequent. A review of the sections previously obtained (July 24) revealed that this specimen also contained numerous identical bodies. Cultures are now in process but are not yet ready for reporting.

Histologic sections were submitted.

### DISCUSSION

DR WILLARD M. MEININGER. This case was of interest because of the rarity of cutaneous torulosis.

The condylomas were unusually extensive. Although verrucae involving mucous membranes have responded well to topical application of 25 per cent resin of podophyllum N F, my colleagues and I have found that the drug has been ineffective in the therapy of verrucae on the skin.

DR L H WINER, Beverly Hills, Calif (by invitation) This case reminds me of pseudoepitheliomatous hyperplasia (White, C, and Weedman, F D Pseudo-Epitheliomatous Hyperplasia at Margins of Cutaneous Ulcers, *J A M A* **88** 1959 [June 18] 1927 Montgomery, H, and Holman, J C *Proc Staff Meet Mayo Clin* **13** 465, 1938 Winer, L H Pseudoepitheliomatous Hyperplasia, *ARCH DERMAT & SYPH* **42** 856 [Nov] 1940) I did not recognize torulas until they were pointed out to me. I did not know what these cells were that I was looking at.

Clinically, the lesions on the back of the neck did not impress me as carcinoma. Microscopically, there was acanthosis of the epidermis but no penetration. There were no intraepidermal abscesses, such as one sees in blastomycosis.

I did not see any sections that one could diagnose as Hodgkin's disease. My opinion is that this disease is torulosis in which there is pseudoepitheliomatous hyperplasia.

DR HIRAM E MILLER We have seen a few patients in San Francisco with torular infection of the central nervous system but none with involvement of the skin. Wile (Cutaneous Torulosis, *ARCH DERMAT & SYPH* **31** 58 [Jan] 1935) reported his observations on a patient with torulosis of the skin. The diagnosis was made after death. There are excellent photomicrographs of pathologic material but none of the cutaneous lesions.

Acneform lesions, furunculoid lesions and boardlike plaques are reported as being observed in torular infection of the skin. None of these lesions was present in this patient, unless the areas on the back of the neck might be considered as being furunculoid.

It is of interest that this man has had Hodgkin's disease for a number of years. Many cases of Hodgkin's disease have been reported in the literature in which torulas were observed in the lymph nodes. Organisms which were thought to be torulas also were noted in the lymph nodes of this patient when the sections were reexamined.

DR HARRY J TEMPLETON, Oakland, Calif, The histologic picture of Hodgkin's disease can be produced by various etiologic agents. Twenty years ago I treated a young woman with classic macular secondary syphilis and large lymph nodes in the neck. Two departments of pathology, both surgical and general, made an unqualified diagnosis of Hodgkin's disease on the nodes. Both the eruption and the enlargement of the nodes disappeared after antisyphilitic therapy. She recovered and is well today, twenty years later, after two competent pathologists agreed on the diagnosis of Hodgkin's disease.

DR FRANCES A TORREY My colleagues and I first saw this patient in 1934 and not again until one year ago. When he was treated in 1934, the eczematoid eruptions failed to respond to the usual treatment. The patient disappeared from observation, and the next thing we heard was that surgeons across the Bay had operated on him for a squamous cell epithelioma about a year ago. We have not seen the sections but were told by the pathologists that it was an epithelioma.

## Book Reviews

**Penicillin Its Practical Application** Under the general editorship of Prof Sir Alexander Fleming, M B, B S, F R C S, F R S, Professor of Bacteriology in the University of London, St Mary's Hospital, London First edition Cloth Price \$7 Pp 380, with 59 illustrations Philadelphia The Blakiston Company, 1946

The editor's purpose in furnishing a general guide to the understanding and use of penicillin is well accomplished in this book, which will be found to be a useful general reference source The book is composed of twenty-seven sections, only two of which were written by the editor, Sir Alexander Fleming He wisely had the chapter on the clinical use of penicillin and other sections written by specialists who were well qualified to discuss the use of penicillin in their fields Also, Professor Fleming readily admits that future advances and new developments will result in reconsideration of the subject

So far as the dermatologist is concerned, his special interest and field is briefly and rather conservatively covered in the section written by A C Roxburgh, physician for diseases of the skin, St Bartholomew's Hospital, London When, where and in what preparations he has found penicillin useful in cutaneous diseases is well discussed and simply presented

Other sections contain occasional references to the use of penicillin in diseases that are treated by the dermatologist, especially the section on syphilis, written by G L M McElligott, director, Department of Venereal Diseases, St Mary's Hospital, London, and part of the section on the use of penicillin in children's diseases, by Donald Paterson, M D, Physician, Hospital for Sick Children

The first one hundred and thirty-four pages of the book are of value because they are well written and cover the subject in general, including the "history and development of penicillin" and the "bacteriological control of penicillin therapy," by Fleming, also the "chemistry and manufacture of penicillin," by A L Bachrach, M A, and B A Hems, Ph D, "pharmacology of penicillin," written by L P Garrod, M D, and, finally, "methods of administration," written by W Howard Hughes, M D All these sections bring out interesting and useful points about penicillin and give a readily available source of information about such things as the technic for estimating the penicillin sensitivity of the infecting organism

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## PENICILLIN IN THE TREATMENT OF EXPERIMENTAL SYPHILIS OF RABBITS

I The Therapeutic Activity of Penicillin in Single and Multiple Doses in Isotonic  
Solution of Sodium Chloride and Peanut Oil-Beeswax  
by Intramuscular Injection

JOHN A. KOLMER, M.D.

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Research Institute of Cutaneous Medicine

With the Technical Assistance of ANNA M. RULE  
PHILADELPHIA

STUDIES bearing on penicillin in the treatment of experimental syphilis of rabbits are of value in relation to the treatment of human syphilis, as has been found true of the organic arsenical and bismuth compounds. Not only are the clinical effects of the compound on acute testicular and cutaneous lesions and on spirochetes in these lesions readily observed by means of dark field examinations, but dosage in relation to complete or biologic cure may be determined with a fair degree of accuracy by means of transfer of lymph nodes.

### PRINCIPLES INVOLVED

It is true that the total dosage of penicillin per kilogram of weight required for the biologic cure of acute testicular syphilis of rabbits is much less than that required for the treatment of early syphilis of human beings. However, valuable information may be gained in relation to methods of administration, the relative therapeutic effectiveness of penicillins F, G, X and K and similar factors. Thus Mahoney, Arnold and Harris,<sup>1</sup> who first discovered the activity of penicillin against *Treponema pallidum* in the treatment of experimental syphilis of rabbits, stated that their early results indicated that the time-dose relationship would have an important bearing on penicillin therapy, and this observation has been amply confirmed. All investigators in the United States have apparently used the same Nichols-Hough strain of *T. pallidum*, with the result that this factor has been held constant, although the time elapsing between

From the Research Institute of Cutaneous Medicine

<sup>1</sup> Mahoney, J. F., Arnold, R. C., and Harris, A. Penicillin Treatment of Early Syphilis, *Am J Pub Health* **33** 1387 (Dec) 1943

inoculation of the testicles and the institution of treatment has varied, as, likewise, the time elapsing after the cessation of treatment before transfers of lymph nodes were made and the period of observation thereafter in relation to complete or biologic cure as well

Indeed, the time-dosage factor has such an important influence on the total dosage per kilogram of weight required for the biologic cure of rabbits that it is difficult to correlate the results observed by different investigators. For example, Raiziss<sup>2</sup> has reported that 1 rabbit given two doses of 2,500 units each in aqueous solution per kilogram twice daily for eight days in succession (40,000 units) showed biologic cure, as, likewise, 1 rabbit given 3,300 units in aqueous solution per kilogram three times a day for eight days in succession (79,200 units). Incidentally, Raiziss also observed that penicillin administered intramuscularly in peanut oil to 4 rabbits was somewhat more effective than intramuscular injections of the compound in aqueous solutions, an observation which has been amply confirmed by our experiments herewith reported. Ercoli and Lafferty,<sup>3</sup> on the other hand, have reported that total doses as high as 132,000 to 282,000 units of sodium penicillin per kilogram, divided into four to six intravenous injections, were insufficient for complete biologic cure of rabbits on the basis of transfer of lymph nodes, while Eagle, Magnuson and Fleischman<sup>4</sup> stated that 10,000 units in aqueous solution by intramuscular injection per kilogram twice daily for four days (80,000 units) cured 90 per cent of rabbits, as, likewise, 400 units per kilogram given five times daily for four days (8,000 units). Furthermore, it is highly probable that the results reported have been greatly influenced by the amounts of penicillins G and X present in the sodium salts of penicillin employed with special reference to penicillin G.

#### METHODS AND MATERIALS

In our experiments all rabbits were inoculated intratesticularly with the Nichols-Hough strain of *T. pallidum*. Acute orchitis developed in all, with strongly positive results on dark field examinations about five to six weeks thereafter, when treatment was instituted. Dark field examinations were then made once a day for three days in succession and thereafter once a week over a total period of seventy days. At the expiration of this period the popliteal lymph nodes of all treated animals were inoculated into the testicles of fresh animals, which were kept under observation for a minimum of four months, when the results were evaluated.

2 Raiziss, G. W. Penicillin in Oil Suspension. Bacteriostatic and Spirochetal Agent, *Science* **100** 412 (Nov 3) 1944, The Effect of Penicillin in Experimental Rabbit Syphilis, *ibid* **102** 329 (Sept 28) 1945

3 Ercoli, N., and Lafferty, L. C. The Anti-Spirochetal Activity of Penicillin in Experimental Infections, *Proc Soc Exper Biol & Med* **57** 4 (Oct) 1944

4 Eagle, H., Magnuson, H. J., and Fleischman, R. The Synergistic Action of Penicillin and Mapharsen (Oxophenarsine Hydrochloride) in the Treatment of Experimental Syphilis, *J Ven Dis Inform* **27** 3 (Jan) 1946

The penicillins employed in treatment were amorphous sodium salts supplied by the Commercial Solvents Corporation. One was a commercial product (no 45072102) with an assay potency of 544 units per milligram, containing 88 per cent penicillin G,<sup>5</sup> in the tables it is referred to as "commercial" penicillin. The second (no 45072104) was a purified product with an assay potency of 1,624 units per milligram, containing 92 per cent penicillin G,<sup>5</sup> in the tables it is referred to as "purified" penicillin.

Aqueous solutions of both lots were freshly prepared as required in sterile isotonic solution of sodium chloride containing 10,000 units per cubic centimeter. Suspensions were also prepared in sterile peanut oil and 3 per cent beeswax containing 10,000 units per cubic centimeter, these were kept at 4 C.

All doses were given in terms of units per kilogram of weight by intramuscular injection in the thighs, followed by brief massage.

#### RESULTS OBSERVED

*Single Doses in Isotonic Solution of Sodium Chloride* As shown in table 1, rabbits were given single intramuscular injections of the commercial and purified penicillins in doses of 10,000, 30,000 and 100,000 units per kilogram, 2 rabbits being treated with each dose respectively. It will be noted that negative results on dark field examinations occurred in about seventy-two hours after each dose, followed by relapsing infections, with positive results from transfers of lymph nodes in every instance. So far as temporarily negative results from dark field examinations are concerned, it will be observed that these effects were more pronounced with the purified than with the commercial penicillin. The single minimal curative dose in isotonic solution of sodium chloride of both penicillins, however, was not determined except to state that it was more than 100,000 units per kilogram of weight.

*Single Doses in Peanut Oil and Beeswax* As shown in table 2, however, the results were much different when similar doses were administered in peanut oil and 3 per cent beeswax. In this experiment a single dose of 10,000 units of the commercial penicillin per kilogram effected the biologic cure of both rabbits and in 1 of 2 animals treated with the purified penicillin. All rabbits treated with single doses of 30,000 and 100,000 units of both penicillins showed biologic cure, so that in these experiments the single minimal curative dose of penicillin in peanut oil and beeswax was approximately 10,000 units per kilogram of weight.

*Multiple Doses in Isotonic Solution of Sodium Chloride* As shown in table 3, both penicillins in isotonic solution of sodium chloride were administered intramuscularly once daily for eight days in succession in doses of 1,000, 5,000 and 25,000 units per kilogram, totaling 8,000, 40,000 and 200,000 units respectively. All 4 animals receiving a total of 8,000 units per kilogram showed temporarily negative results on dark

5 Smith, L. W. Personal communication to the authors.

TABLE 1—Single Doses of Commercial and Purified Penicillin in Isotonic Solution of Sodium Chloride by Intramuscular Injection in the Treatment of Acute Syphilitic Ophthalmia of Rabbits

No	Penicillins	Dose, Units per Kg	Results of Dark Field Examination for T Pallidum, Days *										Results of Transfer of Lymph Nodes			
			1	2	3	7	14	21	28	35	42	49		56	63	70
1	Commercial	10,000	2	1	1	—	4	4	4	4	4	4	4	4	4	Positive
2	Commercial	10,000	2	1	—	—	2	4	4	4	4	4	4	4	4	Positive
3	Commercial	30,000	2	1	—	—	4	4	4	4	4	4	4	4	4	Positive
4	Commercial	30,000	2	1	1	—	4	4	4	4	4	4	4	4	4	Positive
5	Commercial	100,000	2	1	—	—	—	—	—	3	4	4	4	4	4	Positive
6	Commercial	100,000	2	1	—	—	—	—	—	—	4	4	4	4	4	Positive
7	Purified	10,000	4	1	1	—	—	—	—	1	4	4	4	4	4	Positive
8	Purified	10,000	4	1	—	—	—	—	—	2	4	4	4	4	4	Positive
9	Purified	30,000	2	1	—	—	—	—	—	3	4	4	4	4	4	Positive
10	Purified	30,000	2	1	1	—	—	—	—	2	4	4	4	4	4	Positive
11	Purified	100,000	2	1	1	—	—	—	—	2	4	4	4	4	4	Positive
12	Purified	100,000	2	1	—	—	—	—	—	3	4	4	4	4	4	Positive

\* After treatment + indicates large numbers of actively motile spirochetes per dark field, 3, 2 and 1 indicate smaller numbers of spirochetes per dark field respectively, — indicates negative results on dark field examinations

TABLE 2—Single Doses of Commercial and Purified Penicillin in Peanut Oil and Beeswax by Intramuscular Injection in the Treatment of Acute Syphilitic Ophthalmia of Rabbits

No	Penicillins	Dose, Units per kg	Results of Dark Field Examination for T. Pallidum, Days *												Results of Transfer of Lymph Nodes	
			1	2	3	7	14	21	28	35	42	49	56	63		70
1	Commercial	10,000	2	1	1	—	—	—	—	—	—	—	—	—	—	Negative
2	Commercial	10,000	2	1	1	—	—	—	—	—	—	—	—	—	—	Negative
3	Commercial	30,000	2	1	1	—	—	—	—	—	—	—	—	—	—	Negative
4	Commercial	30,000	2	1	1	—	—	—	—	—	—	—	—	—	—	Negative
5	Commercial	100,000	2	1	—	—	—	—	—	—	—	—	—	—	—	Negative
6	Commercial	100,000	2	1	—	—	—	—	—	—	—	—	—	—	—	Negative
7	Purified	10,000	2	1	—	—	—	—	—	—	—	—	—	—	—	Positive
8	Purified	10,000	2	1	1	—	—	—	—	—	—	—	—	—	—	Negative
9	Purified	30,000	2	1	1	—	—	—	—	—	—	—	—	—	—	Negative
10	Purified	30,000	2	1	—	—	—	—	—	—	—	—	—	—	—	Negative
11	Purified	100,000	2	1	—	—	—	—	—	—	—	—	—	—	—	Negative
12	Purified	100,000	2	1	—	—	—	—	—	—	—	—	—	—	—	Negative

\* After treatment + indicates large numbers of actively motile spirochetes per dark field, 3, 2 and 1 indicate smaller numbers of spirochetes per dark field respectively, — indicates negative results on dark field examinations

field examinations, but all relapsed, with positive results on transfer of lymph nodes. Both animals given a total of 40,000 units of commercial penicillin showed persistently negative results on dark field examinations but positive results on transfer of lymph nodes, both animals given 40,000 units of purified penicillin likewise showed persistently negative results on dark field examinations, but 1 showed a negative result on transfer of a lymph gland. All 4 animals given 200,000 units showed persistently negative results on dark field examinations and negative results on transfer of lymph nodes. In the circumstances the minimal curative dose of penicillin in these experiments by intramuscular injection once a day for eight days in succession was in the neighborhood of 5,000 units per dose, totaling 40,000 units per kilogram of weight.

Much different results, however, were observed when the same doses were given twice daily for eight days in succession, as shown in table 4. In this experiment both rabbits given 1,000 units of commercial penicillin per kilogram (totaling 16,000 units) showed biologic cure, with similar results observed in 1 of 2 rabbits given purified penicillin. All 4 animals given a total of 80,000 units and all 4 given a total of 400,000 units per kilogram also showed biologic cure. In these experiments, therefore, the minimal curative dose of penicillin by intramuscular injection twice daily for eight days in succession was approximately 1,000 units per kilogram, totaling 16,000 units.

*Multiple Doses in Peanut Oil and Beeswax* As in the case of single doses however, much better therapeutic results were observed when both penicillins were administered in the same multiple doses suspended in peanut oil and 3 per cent beeswax. Thus, as shown in table 5, the effects on results of dark field examinations were more pronounced. Furthermore, both rabbits given 1,000 units of commercial penicillin per kilogram once a day for eight days in succession (8,000 units) showed biologic cure, with a similar result in 1 of 2 rabbits given purified penicillin. All 4 rabbits given a total dosage of 40,000 units per kilogram also showed biologic cure, and the same results were observed in all 4 given a total dosage of 200,000 units per kilogram. In the circumstances the minimal curative dose of penicillin by intramuscular injection in peanut oil and beeswax once a day for eight days in succession was approximately 1,000 units per kilogram, totaling 8,000 units.

In a second experiment the same doses were given intramuscularly twice daily for eight days in succession, totaling 16,000, 80,000 and 400,000 units per kilogram respectively. As shown in table 6, all animals showed persistently negative results on dark field examinations after the first two to three days of treatment and all yielded negative results on transfer of lymph nodes. In the circumstances the minimal curative dose of penicillin in peanut oil and beeswax by intramuscular injection twice daily for eight days in succession was less than 1,000 units, totaling less than 16,000 units per kilogram of weight.

TABLE 3—Multiple Doses of Commercial and Purified Penicillins in Isotonic Solution of Sodium Chloride by Intramuscular Injection in the Treatment of Acute Syphilitic Orchitis of Rabbits

No	Penicillins	Dose,* Units per Kg	Total Dosage, Units	Results of Dark Field Examination for T <sub>+</sub> Pallidum, Days †												Results of Transfer of Lymph Nodes	
				1	2	3	7	14	21	28	35	42	49	56	63		70
1	Commercial	1,000	8,000	2	1	1	—	—	—	—	—	—	—	4	4	4	Positive
2	Commercial	1,000	8,000	2	2	1	—	—	—	—	—	—	—	4	4	4	Positive
3	Commercial	5,000	40,000	2	1	1	—	—	—	—	—	—	—	—	—	—	Positive
4	Commercial	5,000	40,000	2	1	—	—	—	—	—	—	—	—	—	—	—	Positive
5	Commercial	25,000	200,000	2	1	—	—	—	—	—	—	—	—	—	—	—	Negative
6	Commercial	25,000	200,000	2	1	—	—	—	—	—	—	—	—	—	—	—	Negative
7	Purified	1,000	8,000	2	1	1	—	—	—	—	—	—	—	—	4	4	Positive
8	Purified	1,000	8,000	2	1	1	—	—	—	—	—	—	—	—	4	4	Positive
9	Purified	5,000	40,000	2	1	1	—	—	—	—	—	—	—	—	—	—	Positive
10	Purified	5,000	40,000	2	1	—	—	—	—	—	—	—	—	—	—	—	Negative
11	Purified	25,000	200,000	2	1	—	—	—	—	—	—	—	—	—	—	—	Negative
12	Purified	25,000	200,000	2	1	—	—	—	—	—	—	—	—	—	—	—	Negative

\* Once daily for eight days in succession

† After institution of treatment † indicates large numbers of actively motile spirochetes per dark field examination 3, 2 and 1 indicate smaller numbers of spirochetes per dark field respectively, — indicates negative results in dark field examinations

TABLE 4—Multiple Doses of Commercial and Purified Penicillins in Isotonic Solution of Sodium Chloride by Intramuscular Injection in the Treatment of Acute Syphilitic Orchitis of Rabbits

No	Penicillins	Dose,* Units per Kg	Total Dosage, Units	Results of Dark Field Examination for T <sup>+</sup> Pallidum, Days †												Results of Transfer of Lymph Nodes	
				1	2	3	7	14	21	28	35	42	49	56	63		70
1	Commercial	1,000	16,000	4	1	1	—	—	—	—	—	—	—	—	—	—	Negative
2	Commercial	1,000	16,000	2	1	1	—	—	—	—	—	—	—	—	—	—	Negative
3	Commercial	5,000	80,000	2	1	1	—	—	—	—	—	—	—	—	—	—	Negative
4	Commercial	5,000	80,000	2	1	—	—	—	—	—	—	—	—	—	—	—	Negative
5	Commercial	25,000	400,000	1	—	—	—	—	—	—	—	—	—	—	—	—	Negative
6	Commercial	25,000	400,000	1	1	—	—	—	—	—	—	—	—	—	—	—	Negative
7	Purified	1,000	16,000	4	1	1	—	—	—	—	—	—	—	—	—	—	Positive
8	Purified	1,000	16,000	2	1	—	—	—	—	—	—	—	—	—	—	—	Negative
9	Purified	5,000	80,000	2	1	—	—	—	—	—	—	—	—	—	—	—	Negative
10	Purified	5,000	80,000	1	1	—	—	—	—	—	—	—	—	—	—	—	Negative
11	Purified	25,000	400,000	1	—	—	—	—	—	—	—	—	—	—	—	—	Negative
12	Purified	25,000	400,000	1	1	—	—	—	—	—	—	—	—	—	—	—	Negative

\* Twice daily for eight days in succession

† After institution of treatment † indicates large numbers of actively motile spirochetes per dark field examination, 3, 2 and 1 indicate smaller numbers of spirochetes per dark field respectively, — indicates negative results in dark field examinations

TABLE 5—Multiple Doses of Commercial and Purified Penicillins in Peanut Oil and Beeswax by Intramuscular Injection in the Treatment of Acute Syphilitic Oculitis of Rabbits

No	Penicillins	Dose,* Units per kg	Total Dosage, Units per kg	Results of Dark Field Examination for T. Pallidum, Days †										Results of Transfer of Lymph Nodes			
				1	2	3	7	14	21	28	35	42	49		56	63	70
1	Commercial	1,000	8,000	2	1	1	—	—	—	—	—	—	—	—	—	—	Negative
2	Commercial	1,000	8,000	2	2	1	—	—	—	—	—	—	—	—	—	—	Negative
3	Commercial	5,000	10,000	1	1	—	—	—	—	—	—	—	—	—	—	—	Negative
4	Commercial	5,000	10,000	1	1	—	—	—	—	—	—	—	—	—	—	—	Negative
5	Commercial	25,000	200,000	1	—	—	—	—	—	—	—	—	—	—	—	—	Negative
6	Commercial	25,000	200,000	1	1	—	—	—	—	—	—	—	—	2	2	3	Positive
7	Purified	1,000	8,000	4	1	1	—	—	—	—	—	—	—	—	—	—	Negative
8	Purified	1,000	8,000	4	1	—	—	—	—	—	—	—	—	—	—	—	Negative
9	Purified	5,000	10,000	2	1	—	—	—	—	—	—	—	—	—	—	—	Negative
10	Purified	5,000	10,000	2	1	—	—	—	—	—	—	—	—	—	—	—	Negative
11	Purified	25,000	200,000	1	1	—	—	—	—	—	—	—	—	—	—	—	Negative
12	Purified	25,000	200,000	1	1	—	—	—	—	—	—	—	—	—	—	—	Negative

\* Once daily for eight days in succession

† After institution of treatment. † Indicates large numbers of actively motile spirochetes per dark field examination, †, 2 and 1 indicate smaller numbers of spirochetes per dark field respectively, — indicates negative results in dark field examinations

TABLE 6—Multiple Doses of Commercial and Purified Penicillins in Peanut Oil and Beeswax by Intramuscular Injection in the Treatment of Acute Syphilitic Oculitis of Rabbits

No	Penicillin	Dose,* Units per Kg	Total Dosage, Units per Kg	Results of Dark Field Examination for T. Pallidum, Days †										Results of Transfer of Lymph Nodes			
				1	2	3	7	14	21	28	35	42	49		56	63	70
1	Commercial	1,000	16,000	1	1	1	—	—	—	—	—	—	—	—	—	—	Negative
2	Commercial	1,000	16,000	1	1	1	—	—	—	—	—	—	—	—	—	—	Negative
3	Commercial	5,000	80,000	2	1	—	—	—	—	—	—	—	—	—	—	—	Negative
4	Commercial	5,000	80,000	2	1	—	—	—	—	—	—	—	—	—	—	—	Negative
5	Commercial	25,000	400,000	1	1	—	—	—	—	—	—	—	—	—	—	—	Negative
6	Commercial	25,000	400,000	1	1	—	—	—	—	—	—	—	—	—	—	—	Negative
7	Purified	1,000	16,000	4	2	1	—	—	—	—	—	—	—	—	—	—	Negative
8	Purified	1,000	16,000	4	1	1	—	—	—	—	—	—	—	—	—	—	Negative
9	Purified	5,000	80,000	2	2	1	—	—	—	—	—	—	—	—	—	—	Negative
10	Purified	5,000	80,000	2	1	—	—	—	—	—	—	—	—	—	—	—	Negative
11	Purified	25,000	400,000	1	1	—	—	—	—	—	—	—	—	—	—	—	Negative
12	Purified	25,000	400,000	1	1	—	—	—	—	—	—	—	—	—	—	—	Negative

\* Twice daily for eight days in succession

† After institution of treatment. † Indicates large numbers of actively motile spirochetes per dark field examination, †, 2 and 1 indicate smaller numbers of spirochetes per dark field respectively, — indicates negative results in dark field examinations

## SUMMARY

1 In the treatment of acute syphilitic orchitis of rabbits the minimal single curative dose of commercial and purified amorphous sodium salts of penicillin in isotonic solution of sodium chloride by intramuscular injection was more than 100,000 units per kilogram of weight

2 The single minimum curative dose of the penicillins suspended in sterile peanut oil and beeswax by intramuscular injection, however, was approximately 10,000 units per kilogram of weight

3 The minimal curative dose of the penicillins in isotonic solution of sodium chloride given intramuscularly once a day for eight days in succession was approximately 5,000 units per dose per kilogram, totaling 40,000 units

4 The minimal curative dose of the penicillins in isotonic solution of sodium chloride given intramuscularly twice daily for eight days in succession was approximately 1,000 units per dose per kilogram totaling 16,000 units

5 The minimal curative dose of the penicillins suspended in sterile peanut oil and beeswax by intramuscular injection once a day for eight days in succession was approximately 1,000 units per dose per kilogram, totaling 8,000 units

6 The minimal curative dose of the penicillins suspended in sterile peanut oil and beeswax by intramuscular injection twice daily for eight days in succession was less than 1,000 units per dose per kilogram, or less than a total of 16,000 units

7 Penicillin suspended in peanut oil and beeswax by intramuscular injection, therefore, was found to be therapeutically more effective in the treatment of acute syphilitic orchitis of rabbits than that administered dissolved in isotonic solution of sodium chloride by intramuscular injection

8 The commercial penicillin employed contained approximately 88 per cent penicillin G and the purified penicillin approximately 92 per cent penicillin G

9 So far as these experiments are concerned the results observed with commercial and purified lots of sodium penicillin were closely similar

## ACANTHOSIS NIGRICANS JUVENILIS ASSOCIATED WITH OBESITY

Report of a Case, with Observations on Endocrine Dysfunction in  
Benign Acanthosis Nigricans

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AND

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LOS ANGELES

**A**CANTHOSIS nigricans has been a disease of interest to dermatologists and internists since it was first independently described in 1890 by Pollitzer<sup>1</sup> and Janovsky<sup>2</sup>. Reports of about 400 cases of acanthosis nigricans have appeared to date in the medical literature<sup>3</sup>. The conditions in these cases have been divided almost equally into the adult type, occurring in persons after the age of 20 years, which is usually associated with intra-abdominal malignant growth, and the juvenile benign type, occurring in persons under 20 years of age, without evidence of internal malignant growth. According to Curth,<sup>3c</sup> however, no strict dividing line in age is possible between the so-called malignant and benign forms of acanthosis nigricans, as in some of the cases of the juvenile type either an internal malignant growth has developed while the patient was under 20 years of age or an internal malignant growth has appeared later in adult life. In the majority of the cases reported, the condition has been associated with no internal pathologic changes, and the cause of the disease is considered to be unknown. Numerous hypotheses and theories concerning the cause of juvenile and benign acanthosis nigricans have been advanced by investigators since the earliest reports have appeared. Pollitzer<sup>1</sup> considered the cause to be due to intra-abdominal

From the Department of Dermatology of the University of Southern California School of Medicine

1 Pollitzer, S, in *Internationaler Atlas von seltener Hautkrankheiten*, Leipzig, Leopold Voss, 1890, plate 10

2 Janovsky, V, in *Internationaler Atlas von seltener Hautkrankheiten*, Leipzig, Leopold Voss, 1890, plate 11

3 (a) Moncorps, C. Acanthosis Nigricans, in Jadassohn, J. *Handbuch der Haut- und Geschlechtskrankheiten*, Berlin, Julius Springer, 1931, vol 8, pt. 2, p 372. Bibliography of papers on acanthosis nigricans published before 1931. (b) Michy, J. L'acanthosis nigricans et ses rapports avec les tumeurs malignes, in *Monographies sur les tumeurs*, Laboratoire du Professeur Peyron, Institut Pasteur, Paris, E Le François, 1932, no 12. (c) Curth, H O. Cancer Associated with Acanthosis Nigricans, *Arch Surg* 47 517 (Dec) 1943

fibrous bands, adhesions and congenital malformations Janovsky<sup>1</sup> advanced the theory of excessive exposure to heat Porias<sup>4</sup> suggested that the dystrophies of the skin depend on the altered secretion of internal glands and dysfunction of chromaffin tissue Oppenheim and Loeper<sup>5</sup> expressed the opinion that dysfunction or disease of the suprarenal glands was an etiologic factor in acanthosis nigricans Other hypotheses advanced as to the cause of benign acanthosis nigricans have been exposure to cold,<sup>2</sup> syphilis,<sup>6</sup> decapsulation of the kidneys,<sup>7</sup> hepatic cirrhosis<sup>8</sup> and injury or disturbance to the abdominal sympathetic nervous system<sup>9</sup>

It is of interest that no article has appeared in the American dermatologic or medical literature on juvenile acanthosis nigricans associated with obesity The findings of endocrine dysfunction involved in the reported case and in other cases of the juvenile type associated with obesity compiled from the medical literature reveal observations that may be of aid to advance further the knowledge concerning the cause of the benign form of this disease It is the purpose of this paper to report a case of acanthosis nigricans juvenilis associated with obesity, to present a compilation of cases of this type from the reports in the medical literature and to discuss the dysfunction of the endocrine gland associated with the benign type of this disease

#### REPORT OF A CASE

*History*.—M P, a 17 year old school boy, was examined because of a pigmented eruption on the neck, axillas and crurogenital area of three years' duration Similar lesions had recently appeared on the forehead, chest, back and hands No subjective symptoms were associated with the eruption During the preceding few months the pigmented areas had darkened, roughened and slowly spread No other members of his family suffer from cutaneous disease The patient has been obese since early childhood His weight at birth was 5 pounds 7 ounces (2,477 Gm) At 5 years of age he was 20 pounds (9.09 Kg) overweight, short in stature and had "stubby" fat hands At 7 years he weighed 88½ pounds (41 Kg) and his height was 50 inches (127 cm) A roentgenogram of both wrists at the age of 7 years showed retarded epiphysial development, and a diagnosis of Frohlich's syndrome was made by an endocrinologist Intensive endocrine therapy with posterior pituitary injection and two proprietary preparations of chorionic gonadotropin was administered from April 1935 to June 1937,

4 Porias, J Ueber die Beziehungen der Akanthosis nigricans zu malignen Tumoren, Wien klin Rundschau **27** 671, 1913

5 Oppenheim, R, and Loeper, M L'insuffisance surrenale experimentale par lesions directes des capsules, Compt rend Soc de biol **55** 332, 1903

6 de Azua, J Acanthosis Nigricans, J Cutan Dis **31** 966, 1913

7 Wise, F Acanthosis Nigricans Following Decapsulation of the Kidneys, J Cutan Dis **36** 35, 1918

8 Crocker, cited by Moncorps<sup>2a</sup>

9 (a) Wile, U, in discussion on Wieder<sup>18</sup> (b) Masson, J C, and Montgomery, H Relationship of Acanthosis Nigricans to Abdominal Malignancy, Am J Obst & Gynec **32** 717, 1936

without retarding the patient's progressive obesity. At the age of 8 years his weight was 111 pounds (53 Kg.) and his height was 51½ inches (130.8 cm). At the age of 9 years his weight was 130 pounds (59 Kg.) and his height was 55 inches (139.7 cm). The patient's present weight is 315 pounds (143.2 Kg.), and his height is 5 feet 9 inches (175.2 cm). His mental development has been normal, and he is of average intelligence. His father is obese, and his mother suffers from pituitary type of obesity. One brother, aged 15 years, is obese and weighs 200 pounds (91 Kg.).

*Physical Examination*—The patient was a well developed obese young man who appeared to be of stated age. The hair was normal in distribution and texture.

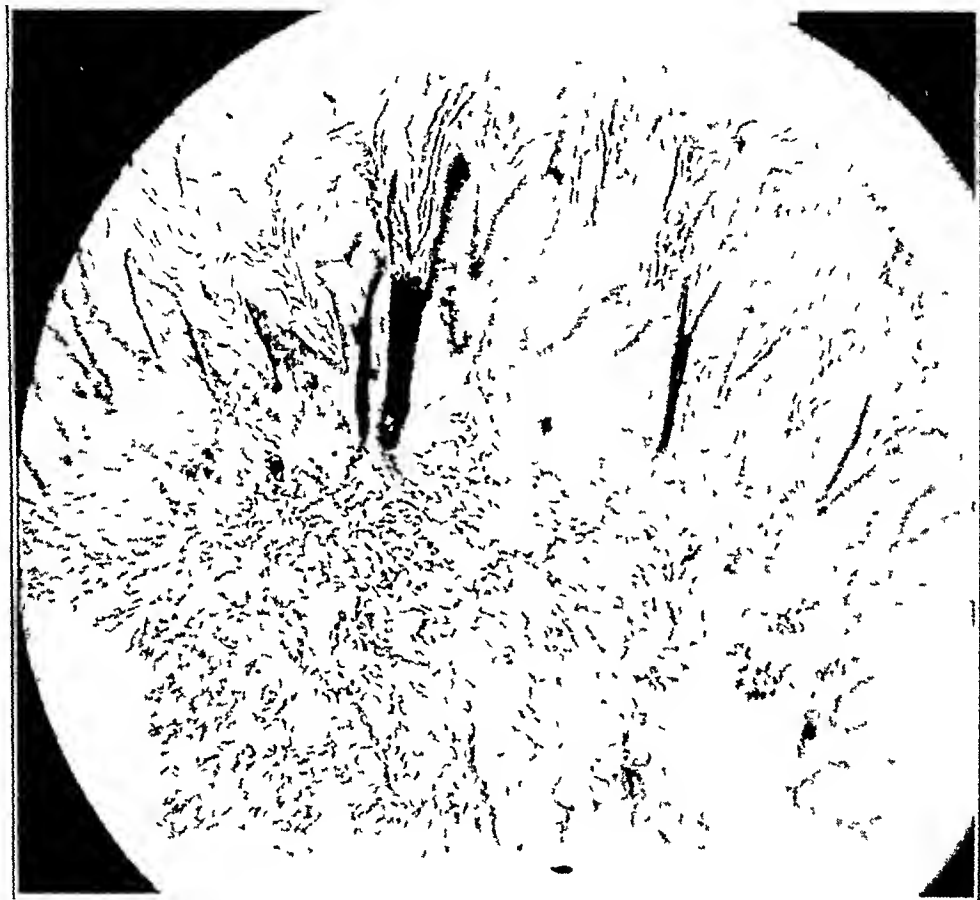


Fig 1—Acanthosis nigricans, juvenile type. Photomicrograph (low power) of section of skin from the axilla, showing hyperkeratosis, acanthosis, increased pigment granules in basal cell layer and decided papillary hypertrophy.

The obesity was especially located in the abdominal region, with an apron-like pendulous distribution. The hands were short and stubby, with shortened thick fingers. The finger nails were irregular and discolored and broken off in their distal portions. The genitals showed normal development. The heart, lungs and nervous system were normal. The examination of the abdomen showed no masses or areas of tenderness. The spleen and liver were not palpable. The blood pressure was 160 systolic and 86 diastolic.

*Dermatologic Examination*—A diffuse brownish black hyperkeratotic plaque-like papular eruption was located on the forehead, neck, axillae, upper part of the chest, lower part of the back, dorsa of the hands and genitocrural regions. The

skin of the axillas and inguinal regions was thickened and furrowed. Numerous small discrete elevated brownish verrucae and papules were superimposed on the pigmented axillary patches. Some of these papillomas were pedunculated. On the chest and back were numerous discrete, superficial, brownish, macular, scaling lesions. Superimposed on the pigmented furrowed skin of the left groin and extending to the lower part of the abdomen was an annular palm-sized lesion with a papulovesicular scaling raised border and a clear center. The lips, tongue and oral mucous membranes were normal.

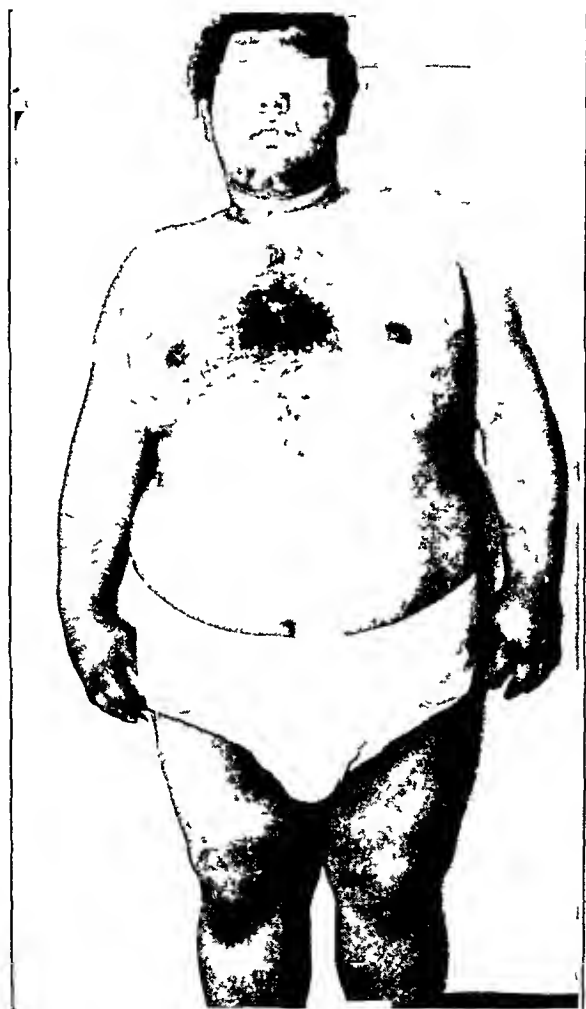


Fig 2—Acanthosis nigricans, juvenile type, associated with obesity

*Laboratory Examinations*—The Wassermann and Kahn tests of the blood elicited negative serologic reactions for syphilis. Examination of the blood showed a hemoglobin content of 82 per cent, a color index of 0.9, 4,600,000 erythrocytes and 6,800 leukocytes with 77 per cent neutrophils, 17 per cent lymphocytes, 4 per cent monocytes and 2 per cent eosinophils. The dextrose tolerance test by the two dose method of Exton and Rose gave results as follows: fasting specimen, 89 mg per hundred cubic centimeters; one-half hour after ingestion of the first dose (50

Gm) of dextrose, 130 mg, and one-half hour after ingestion of the second dose (50 Gm) of dextrose, 112 mg. The examination of the blood plasma for ascorbic acid showed 0.4 mg per hundred cubic centimeters, compared with the normal value of 0.8 to 2.4 mg. The result of a basal metabolic test was plus 8 per cent. The urine was normal. Roentgenograms of the skull showed the sella turcica to be normal in size and shape, with normal clinoid processes.

*Histologic Examination*—A biopsy specimen from the right axilla was stained with hematoxylin and eosin. The epidermis showed relative and absolute



Fig. 3—Acanthosis nigricans, juvenile type, showing involvement of the lateral surface of the neck

hyperkeratosis with irregular acanthosis and adjacent areas of atrophy of the rete cell layer. The papillary bodies were elongated and narrow. The basal layer of the epidermis contained considerable melanin pigment. Examination of the cutis showed occasional chromatophores laden with melanin pigment. No inflammatory reaction or disturbance of the connective tissue could be found in the corium. The blood vessels and subcutaneous fat tissue were normal. The microscopic diagnosis was acanthosis nigricans.

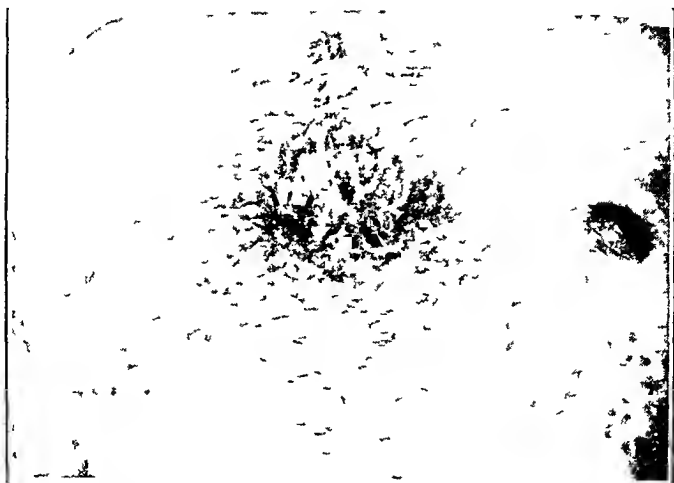


Fig 4—*Acanthosis nigricans*, juvenile type, showing involvement of the chest. The lesions of *tinea versicolor* are superimposed on the pigmented patches of *acanthosis nigricans*.



Fig 5—*Acanthosis nigricans*, juvenile type, showing axillary involvement with papillomas.

Microscopic examination of scrapings from the superficial macular lesions of the back and chest revealed *Microsporon furfur*. Scrapings from the elevated border of the annular lesion on the groin examined microscopically revealed myceliums and spores of dermatophytosis. Scrapings from the nails were negative for fungi on microscopic examination and culture.

The clinical and laboratory diagnosis was juvenile acanthosis nigricans associated with obesity of endocrine type, tinea versicolor of the trunk and dermatophytosis involving the crural and abdominal regions.

*Treatment*—The patient was given a restricted diet, and a salicylic acid exfoliating cream was prescribed for the pigmented areas. Because of the low level of ascorbic acid in the blood, ascorbic acid in high dosage was administered orally and intramuscularly. No beneficial effects were noted in the cutaneous picture as a result of this therapy. The tinea versicolor on the trunk and the

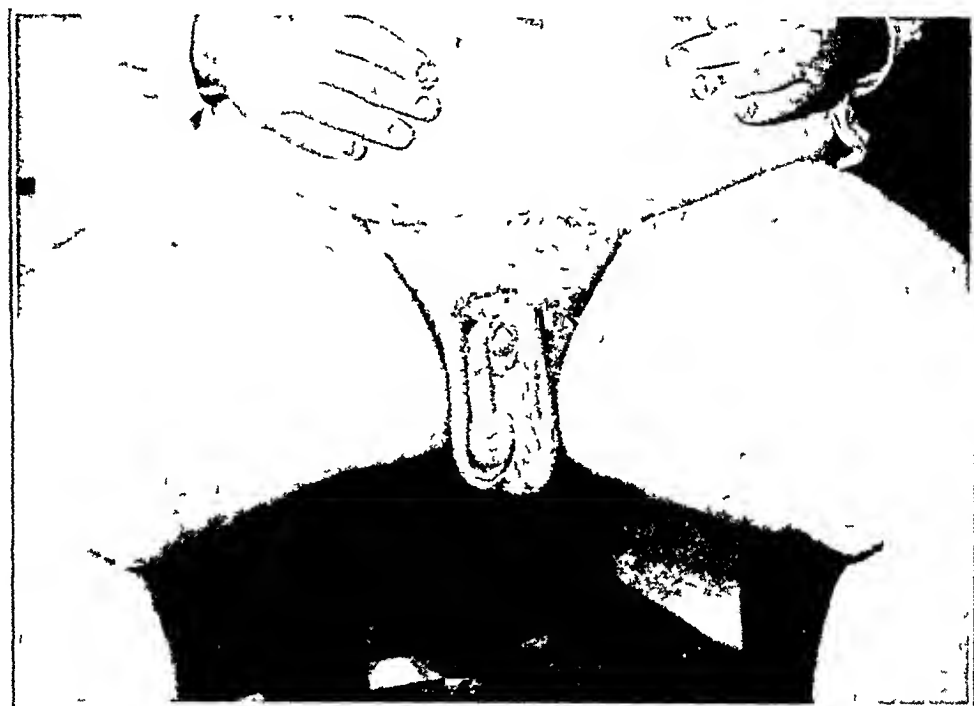


Fig 6—Acanthosis nigricans, juvenile type, showing increased pigmentation and hyperkeratosis about the crurogenital region. The pigmented patches on the dorsa of the hands and the dyskeratotic finger nails can be seen.

dermatophytosis in the groin were treated with a fungicidal ointment. The mycotic infections cleared readily, but there was no gross change in the underlying patches of acanthosis nigricans.

#### COMMENT

The cause of the adult type of acanthosis nigricans has been accepted by most investigators<sup>10</sup> to be due to an internal malignant growth affecting the suprarenal glands and chromaffin system. The malignant growth in almost all cases has been intra-abdominal in origin and commonly originates in the stomach. Malignant growths associated with acanthosis nigricans that occur primarily outside of the abdominal cavity include

<sup>10</sup> Curth<sup>3c</sup> Wile<sup>21</sup>

those having origin in the breast <sup>11</sup> and lungs <sup>12</sup> Regardless of its origin, the malignant growth commonly metastasizes to the splanchnic region of the abdomen, especially the suprarenals The cause of the juvenile or benign form of acanthosis nigricans has been obscure Most of the recorded cases of benign conditions have had no mention of associated internal pathologic changes or abnormal metabolism A compilation was made of reports of cases of benign acanthosis nigricans associated with dysfunction of the endocrine gland (table 1) Examination of this compilation shows dysfunction of the endocrine gland to be a common finding associated with the benign type of this disease when internal pathologic or metabolic disorders are found Among the ductless glands reported <sup>3a, c</sup> to have disturbances associated with benign acanthosis nigricans are the thyroid, thymus, chromaffin system, pituitary body, pancreas, suprarenals and gonads No single type of dysfunction of the endocrine gland has been found consistently in benign forms of the condition This lack of association of a single definite type of disturbance of the endocrine gland has led Curth <sup>13</sup> and Grace and Schwartz <sup>14</sup> to oppose the belief that endocrine dysfunction is an etiologic basis for the disease In support of their belief, Grace and Schwartz pointed out that no endocrine disturbance is known to produce cutaneous changes similar to those found in acanthosis nigricans and that organotherapy is of no value in benign forms or others Knowles, Sidlick and Ludy <sup>15</sup> likewise did not consider disease or functional disturbance of the suprarenal glands in itself to be responsible for the cutaneous picture of acanthosis nigricans Among investigators who considered benign acanthosis nigricans to be due to endocrine dysfunction are Hellerstrom,<sup>16</sup> Smith <sup>17</sup> and Wieder <sup>18</sup> Hellerstrom stated the belief that the endocrine character of benign acanthosis nigricans is demonstrated by its retrogression after castration in a patient who also suffers from severe diabetes mellitus Smith's patient with benign acanthosis nigricans also suffered from acroinegalic gigantism, a dis-

11 Curth <sup>3c</sup> Masson and Montgomery <sup>9b</sup>

12 Cited by Curth <sup>3c</sup>

13 Curth, H O Benign Type of Acanthosis Nigricans Etiology, Arch Dermat & Syph **34** 353 (Sept) 1936, footnote 3c

14 Grace, A W, and Schwartz, H J Acanthosis Nigricans Case of Benign Form in Adult Investigated from Aspect of Endocrine Dysfunction, Arch Dermat & Syph **29** 691 (May) 1934

15 Knowles, F S, Sidlick, D M, and Ludy, J B Acanthosis Nigricans Arch Dermat & Syph **19** 391 (March) 1929

16 Hellerstrom, S Zur Kenntnis der Acanthosis nigricans, Acta dermat-venereol **14** 86 1933

17 Smith, S W A Case of Juvenile Acanthosis Nigricans, Brit J Dermat **45** 142, 1933

18 Wieder L M Acanthosis Nigricans, Juvenile Type, J A M A **87** 1964 (Dec 11) 1926

TABLE 1—*Reports of Benign Acanthosis Nigricans Associated with Dysfunction of the Endocrine Gland*

Authors

Kemerl, D  
Patrassi, G

Presented by the Mayo Clinic  
Knowles, F O, and Ludy, J B

Behjet, H

Masson, J O, and Montgomery, H  
(cases 1, 9 and 10)  
Perman, B (case 3)  
Flackamp, W

Miescher, G

Mullan, G J

Ravogli, A

Hermans, E H, and Schokking, C R  
Pollitzer, S

Lawrence, R D

Hellerstrom, S

Weiss, I

Ottikhine, A T

Goldschlag

Barenblatt, J

Artom, M

Smith, S W

Weider, L M

Disease

Hypothyroidism and dwarfism in 5 members of a family  
of diencephalic origin following psychologic trauma

Hyperthyroidism and exophthalmic goiter  
Hyperthyroidism, basal metabolic rate, minus 15 per cent

Dysfunction of the thyroid gland (goiter)

Adenoma of thyroid gland (goiter)

Dysfunction of the thyroid gland (goiter)

Dysfunction of the thyroid gland (goiter)  
2 cases of congenital familial acanthosis nigricans associated

Diabetes mellitus

Diabetes mellitus

Diabetes mellitus

Diabetes mellitus

Diabetes mellitus (hemochromatosis)

Severe diabetes mellitus (familial)

Crypto orchism

Double crypto orchism

Pluriglandular insufficiency

Pluriglandular insufficiency

Facies hypopituitaria (2 cases)

Acromegalic gigantism, pituitary and suprarenal dysfunction

Hypofunction of suprarenal glands and increased sugar tolerance

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Brit J Dermat 45 142, 1933

J A M A 87 1964, 1926

ordered abdominal sympathetic system and probable suprarenal cortical disease. This investigator considered benign acanthosis nigricans to be a combined disease with origin in the endocrine glands affecting the pituitary body, suprarenal glands and the abdominal sympathetic system. In support of his belief Smith stated that anterior pituitary secretion plus excess suprarenal function is known to occur in the adrenal cortex in both gigantism and acromegaly. Wieder expressed the opinion that hypofunction of suprarenal glands increases tolerance for sugar, because in his case acanthosis nigricans was associated with impairment of secretion of the ductless glands, particularly the suprarenals. Curth,<sup>13</sup> although stating that there is no basis for assuming an endocrine causation in the benign type of the disease, expressed the belief that the common onset and spread of acanthosis nigricans in and through puberty is evidence in favor that "sex hormones play some role in the propagation of the disease." We are in agreement with the foregoing findings and opinions of investigators favoring the relationship of dysfunction of the endocrine glands to benign acanthosis nigricans. We believe that such findings and opinions tend to strengthen one's thoughts that endocrine dysfunction may play an important role in the cause of the benign type of this disease.

A review of the literature revealed the reports of 10 cases of acanthosis nigricans juvenilis associated with obesity (table 2). The geographic distribution of the cases was in Europe, North America and South America. All patients in the group were in the age of puberty, and all except 1 were females. Our patient is the second male patient to be recorded. In some of the cases reported the patients with obesity had a history of familial obesity or familial acanthosis nigricans associated with obesity (table 2, cases 1a and 1b). Our patient likewise had a familial history of obesity. Roentgenograms of the sella turcica have been normal in all cases when reported. Becker and Obermayer (table 2, case 8) recorded that their patient showed a decreased tolerance for dextrose and hypertension on exertion. Our patient likewise was found to have hypertension. Senear's patient (table 2, case 9) suffered from mild hypothyroidism. All other patients in the series had a normal basal metabolic rate when reported and showed no evidence of thyroid dysfunction. Butterworth (table 2, case 7) reported that his obese patient lost weight when given a restricted diet and thyroid extract, with no resultant gross change in the cutaneous picture. Senear and Cornbleet (table 2, case 3) conversely reported that their patient lost 30 pounds (13.6 Kg) by restricted diet, with resultant almost complete involution of the pigmented patches. Two of the 9 females in the series suffered from amenorrhea and dysmenorrhea, but there were no definite findings of ovarian dysfunction. The obesity reported in almost all instances was of pituitary type due to insufficiency of the anterior lobe. The age of onset of obesity when reported, was in early childhood. The obesity

TABLE 2—Reported Cases of *Acanthosis Nigricans Juvenilis* Associated with Obesity

Case No	Age	Sex	Weight and Height	Laboratory Findings (Diagnosis Proved by Histologic Section in Each Case)	Comment	Bibliography
1 a	14	♀	193 lb (83 kg)	Results of sugar tolerance tests normal for both patients	Familial acanthosis nigricans associated with obesity in a mother, daughter and son	Jedassohn, W 110, 1926 Arch f Dermat u Syph 150
b	11	♂	143 lb (65 kg)			
2	16	♀	184½ lb (83½ kg), 5 ft 1½ in (156.27 cm)	None reported	Endocrine dysfunction present	Presented by Dr Wertheimer at the meeting of the Pittsburgh Dermatological Society, June 21, 1928 (Arch Dermat & Syph 19 162, 1929)
3	17	♀	280 lb (127 kg)	Basal metabolic rate minus 10 per cent	Jewish woman with acanthosis nigricans of 2 yr duration onset of copulency at age 9 dysmenorrhea, reduced 30 lb (13.6 kg) by restricted diet in 2 mo with resultant almost complete involution of pigmented acanthosis nigricans patches	Presented by Dr L I Sencar and Dr T Cornbleet at the meeting of the Chicago Dermatological Society, Oct 17, 1928 (Arch Dermat & Syph 19 511, 1929)
4	12	♀	260 lb (117.9 kg)	Roentgenogram of sella tureica normal	Negro woman suffering from endocrine dysfunction	Presented by Dr Ralph and Dr Klauder at the meeting of the Philadelphia Dermatological Society, Dec 3, 1938 (Arch Dermat & Syph 19 323, 1939)
5	17	♀	225 lb (102 kg), 5 ft 6 in (167.6 cm)	Basal metabolic rate plus 10, roentgenogram of sella tureica normal	Lndocrine type in appearance no history of ovarian dysfunction	Presented by Dr H E Mehelson at the meeting of the Minneapolis Dermatological Society, Oct 23, 1930 (Arch Dermat & Syph 23 388, 1931)
6	13	♀	207 lb (94 kg), 5 ft 4½ in (164 cm)	Roentgenogram of sella tureica normal	Scanty menses every 3 or 4 mo	Presented by Dr A Saver at the meeting of the Bronx Dermatological Society, Nov 30, 1936 (Arch Dermat & Syph 36 448, 1937)
7	16	♀	271 lb (104.8 kg)	Basal metabolic rate normal	Obesity considered to be of pituitary type, patient lost 12 lb (5.4 kg) in 5 wk when placed on restricted diet and 2 grams (0.1 gm) of thyroid extract daily there was no gross change in the endocrine picture Patient gained 40 lb (18 kg) in 3 yr obesity had distribution of the pituitary habitus hypertension on exertion, mild diabetes mellitus	Butterworth, T Arch Dermat & Syph 39 552, 1939
8	11	♀	236 lb (106.6 kg)	Reaction to tuberculin test negative, basal metabolic rate normal, decreased tolerance for dextrose	Mild hypothyroidism of 3 yr duration	Presented by Dr S W Becker and Dr M I Ohermayer at the meeting of the Chicago Dermatological Society, May 21, 1941 (Arch Dermat & Syph 47 235, 1942)
9	15	♀	187 lb (85 kg)	Wassermann reaction of the blood positive, roentgenogram of sella tureica normal		Presented by Dr F F Sencar at the meeting of the Chicago Dermatological Society, May 21, 1941 (Arch Dermat & Syph 47 236, 1942)
10	11	♀	169 lb (77 kg)	Basal metabolic rate normal, roentgenogram of sella tureica normal	Idiopathic syndrome type of obesity, familial obesity, acanthosis nigricans of 2 mo duration	Gutman, R, and Saluces, P I Rev argent dermatosif 26 1030, 1942

was of progressive type and usually antedated the acanthosis nigricans by years. The diagnosis made for our patient at the age of 7 was Frohlich's syndrome, and the acanthosis nigricans appeared when he was 14 years old. The pituitary type of obesity associated with juvenile acanthosis nigricans in most cases in our series would tend to support the belief that endocrine disturbance involving the pituitary gland plays a role in the production of this cutaneous picture. Our series of cases is in agreement with that of Curth,<sup>13</sup> that the onset and spread of acanthosis nigricans at the beginning or during the age of puberty would be evidence in favor of the belief that the gonads or sex hormones are also involved in the propagation of the juvenile type of this disease. The association of obesity with juvenile acanthosis nigricans in the recorded cases indicates that one may find mild acanthosis nigricans more frequently in obese adolescents if it is carefully sought for.

#### SUMMARY AND CONCLUSIONS

A case of acanthosis nigricans juvenilis associated with obesity is reported, with a compilation of cases from the medical literature.

Observations on dysfunction of the endocrine glands associated with benign acanthosis nigricans warrant serious consideration that glandular dysfunction, particularly involving the pituitary, suprarenals and gonads, may play an important role in the cause of benign acanthosis nigricans.

The obesity associated with juvenile acanthosis nigricans is usually pituitary in type. The age of onset and spread of juvenile acanthosis nigricans at the beginning or during the age of puberty are evidence in favor of the belief that the gonads or sex hormones play a role in the propagation of the juvenile type of the disease. These findings tend to strengthen our views concerning the importance of endocrine dysfunction involving the pituitary gland and gonads in the benign juvenile type of this disease associated with obesity.

It is our belief that the tinea versicolor and dermatophytosis infections found in our patient were coincidental and had no etiologic relationship to the underlying patches of acanthosis nigricans.

The association of obesity with benign juvenile acanthosis nigricans indicates that a careful search for mild forms of this disease in obese adolescents, particularly those suffering from glandular dysfunction, may reveal cases in which acanthosis nigricans has not been diagnosed.

## MADURA FOOT (MYCETOMA)

First Report from the Isthmus of Panama

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PANAMA, REPUBLIC OF PANAMA

SOME TIME ago it was interesting to note the lack of bibliographic data on actinomycosis on the Isthmus of Panama, whereas there were various reports from Puerto Rico,<sup>1</sup> Cuba<sup>2</sup> the southern part of the United States<sup>3</sup> and Mexico,<sup>4</sup> which, like the isthmus, bound the Caribbean Sea. Also the geographic location of the isthmus, with its warm, humid climate, would appear to make it a favorable region for any type of mycotic infection. The later diagnosis in the first 2 cases of chromoblastomycosis,<sup>5</sup> when I commenced my investigations, and in the third and fourth cases (as yet unreported), observed in the last fifteen months, leads me to believe that actinomycosis can be encoun-

From the medical staff of the Hospital Santo Tomas

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tered on the isthmus in any of its clinical forms, in particular, Madura foot (mycetoma), or that it has been recognized but has not been reported in the past

My study has confirmed my previously indicated suspicions, showing 1 case of actinomycetoma and 1 of thoracic actinomycosis, furthermore, it has shown that in Hospital Santo Tomas since the year 1922 there have been 2 other patients with the diagnosis of Madura foot (although without laboratory examinations) and that in Gorgas Hospital, in the Canal Zone, this same diagnosis has been made in a patient, with pathologic reports and cultures of the strain as confirmation. In several other records (4 cases) there is a suggestion of this disease, however there is no laboratory confirmation nor do the clinical descriptions in these records correspond to the classic picture of Madura foot.

The clinical history of the case of Madura foot I have studied is as follows

#### REPORT OF A CASE

M. A., a 42 year old white man, who still lives in the town of his birthplace, Las Lomas (province of Chiriqui, Republic of Panama), is a farmer and works wearing *cutaria* (sandals). He entered Hospital Santo Tomas with elephantiasis and multiple fistulas with granular, lobulated edges of the left foot, of four years' duration. The history revealed that the disease had commenced shortly after the patient had received a hard blow on the left ankle, which produced ecchymoses, edema and intense pain, requiring four days' rest in bed. The first change that the patient observed was the formation of a small purulent, painless mass over the left metatarsal arch, cyanotic in color, from which dark blood drained on opening of the mass, a crust formed over the mass, and on its removal there was always an abundant serous discharge with a disagreeable odor and occasionally bloody. Eight days later a second pustule developed near the primary lesion, which progressed in the same manner, a third, fourth and even fifth lesion developed, the new one always appearing at the time of formation of the crust of the preceding lesion nearby and with the same physical and subjective characteristics as the primary one. Since then, with periods of regression and exacerbation other lesions have occurred with a slow, chronic progression, without any tendency to spontaneous healing and, on the contrary accompanied with edema of the foot, gradually causing a loss of its normal lines of concavities, the foot has finally become so painful and deformed that walking has been impossible (fig. 1).

His medical history in other respects was noncontributory, with the exception that he had had malaria and an appendectomy for chronic appendicitis.

Physical examination (inspection) revealed an anemic, emaciated person with atrophy of the left thigh and leg as far as the inferior third portion, where there were three scars from previous fistulization, which had healed well. There was a decided increase in the diameter of the left foot where the natural concave appearance had been lost. The toes were moderately edematous (increasing from the big toe to the small toe) and without separation and were at a distinct level from the sole. The surface of the foot was irregular because of multiple, wide-based nodules (none pedunculated), some confluent (easily distinguished by their size), from the majority of which drained a seropurulosanguinous liquid, of a disagreeable odor, with a variable number of yellowish white granules. There were many other nodules, without drainage, that were covered by a thin layer of skin, through which

one could see crystal clear fluid, confirmed by aspiration. The vertex of the nodules corresponded to the site of drainage, each nodular fissure led to the formation of a fistula, which became evident by a central depression and which temporarily might become covered with a crust, the removal of which immediately started new drainage. However, some lesions had healed completely, decreasing in size but becoming harder. I noted that the patient held his foot in semiflexion, and it appeared to be shorter than the right foot, also, the left foot was in valgus position, with the tip of the foot in abduction (the internal malleolus was nearly in an anterior position).

Examination by organs gave essentially normal results in each aspect, with the exception of moderate hypertrophy of the lymph nodes in the left triangle of Scarpa and of the atrophy, previously mentioned, in the lower left extremity, with the following measurements:  $15\frac{4}{10}$ ,  $13\frac{3}{10}$ , 12,  $10\frac{2}{5}$  and  $8\frac{3}{10}$  inches (40, 34, 30, 26 and 21 cm) in the right extremity, in comparison to  $13\frac{1}{2}$ ,  $11\frac{1}{2}$ , 9,  $8\frac{1}{2}$  and 8 inches (34, 29, 22, 21 and 20 cm) respectively in the left extremity, at the levels of middle and inferior thirds of the thigh and at the superior, middle and inferior thirds of the lower leg. The circumference of the diseased foot at its middle portion was  $13\frac{1}{2}$  inches (34 cm), in comparison to  $8\frac{1}{2}$  inches (21 cm) in the normal foot.

*Laboratory Examination*—The urine was normal in all respects. The feces presented eggs of *Uncinaria*, the Kahn reaction was negative. Examination of the blood chemistry for glucose, nonprotein nitrogen, albumin nitrogen and globulin nitrogen, icteric index, van den Bergh reaction and albumin-globulin ratio showed values all within normal limits. There was moderate anemia, of a normocytic hyperchromic type, the platelet count was normal, the sedimentation rate was 37 mm in an hour. A moderate leukocytosis (73 per cent polymorphonuclears) with lymphocytopenia was present. Roentgenograms of the left foot showed that the density of the soft tissues was too great to permit the study in detail of the osseous (fig 2) structures, but one could see necrosis of the calcaneum and general osteoporosis of the bones of the foot, which had advanced as far as the inferior aspect of the tibia and fibula. A roentgenogram of the thorax revealed no pulmonary or cardiovascular changes.

*Histopathology*—The microscopic examination of the excised nodule showed decided acanthosis, with projection of the rete pegs into the underlying tissues. The dermis showed dense fibrous tissue and leukocytic infiltration (especially of the polymorphonuclear type) greater in the papillae about the blood vessels, which showed thickened walls, due to proliferation of their adventitial coats. The subcutaneous tissues showed dense fibrous and hyalinized connective tissue infiltrated with polymorphonuclear leukocytes and macrophage cells, foci of polymorphonuclear cells, unassociated with the presence of fungous organisms, surrounded by fibrous tissue and macrophages, vessels with thick walls surrounded by polymorphonuclear infiltration, small capillaries with diminished lumens due to thickening of its wall, vessels partially occluded (fig 3A) by pink or blue stained-filamentous forms, surrounded by polymorphonuclear leukocytes and macrophages, and ray fungus (fig 3B) stained brown in its central part and pink in the outer zone without definite filamentous forms being visible close to the pink outer zone, as has been described by some investigators, however, "clubs" forms were distinguishable. The ray fungus was always surrounded by a thick layer of polymorphonuclear infiltration, at its periphery were seen granulation tissue heavily infiltrated with polymorphonuclear leukocytes and macrophages and, more peripherally, fibrous tissue infiltrated with plasma cells. In the slides studied no giant cells were encountered.

*Mycologic Examination*—Examination of the granules between slide and cover glass showed the characteristic actinomycotic forms of ray fungus (fig 4) with the club-shaped forms at the periphery and filaments in the central part. The granules were whitish yellow.

Culture of the granules, after being washed in isotonic solution of sodium chloride and cut into small portions, was made on Sabouraud's medium at room



Fig 1—Appearance of the foot at the time of the patient's admission to the hospital, with nodular formations, sinus tracts and moderate elevation of the toes (above the plantar surface)

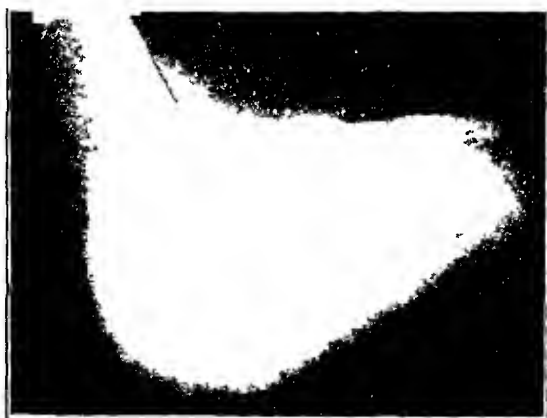


Fig 2—The density of the soft tissues is too great to permit the study in detail of the osseous structures. Nevertheless one can see necrosis of the calcaneum and general osteoporosis of the bones of the foot and inferior aspect of the tibia and fibula.

temperature (28 C [82.4 F]) and at incubator temperature of 37 C (98.6 F). One mycotic colony growing among contaminant staphylococcus colonies was clearly visible after nineteen days' incubation, the surface was wrinkled, of a creamy consistency and whitish yellow, becoming more yellowish with time. Transplantation

of the colony, to obtain a pure culture, showed a definite growth (fig 5) within thirty-six hours of a strain, whitish, moist and always with a wrinkled center, sometimes depressed and other times decidedly elevated. The colony was surrounded generally by a smooth zone with radial striations, frequently outside this zone was

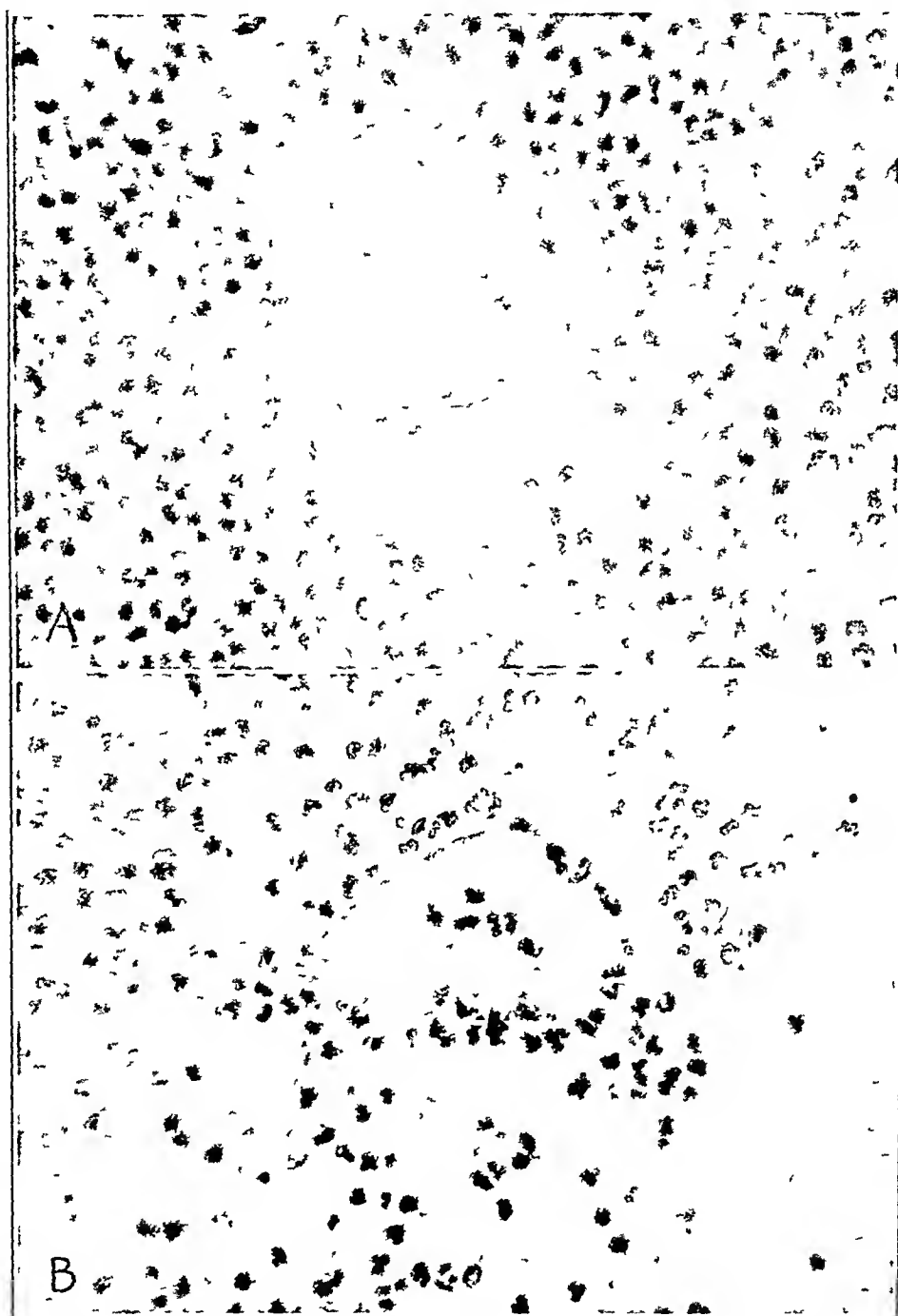


Fig 3—*A*, vessel partially occluded by filamentous forms, surrounded by polymorphonuclear leukocytes and macrophages  $\times 460$ . *B*, ray fungus with its central and outer portions without definite filamentous forms being visible but with characteristic "club" forms at the periphery, surrounded by polymorphonuclear leukocytes and macrophages  $\times 460$ .

seen a third smooth zone, whose edges were slightly elevated. The culture always became more yellow with age, its odor was similar to that of damp earth.

Microscopic examination of the strain growing on the slides showed abundant filament forms, with a nearly imperceptible cellular membrane, nonsegmented, occasionally with refringent granules, branching, without formation of chlamydospores (fig 6) and of variable length. Besides the long filaments one could observe shorter forms, some bacilliform (occasionally with one end wider than the other,



Fig 4—Characteristic actinomycotic forms of the ray fungus, with the "club" forms at the periphery (from the granules)  $\times 120$

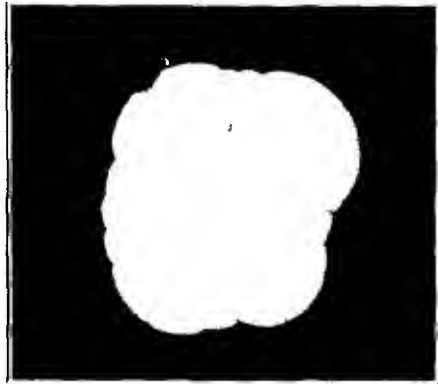


Fig 5—Pure culture at the fourth week of incubation at room temperature (28 C [82.4 F])

especially in the old tubes) and even coccic forms. Also, a few large round forms, of 3 to 4 microns in diameter, were seen (fig 6). Staining of a thin smear of the fungus in suspension of isotonic solution of sodium chloride revealed that the developed organism was not acid fast and that it was gram-positive.

Fermentation tests were employed, with these results (the reading was made at forty-eight hours). There was a fine pellicle with granular growth on the surface

of all the mediums used (glucose saccharose, maltose, mannitol and lactose), no gas formation was present in any of the carbohydrate mediums used, in the bottom of the tubes there was a fine precipitate of granular growth, and, finally, the liquid itself was clear in appearance in all the mediums

With the same purpose I cultured in blood agar at incubator temperature of 37 C, a definite growth was observed within twenty-four hours of a strain with the same microscopic appearance previously reported, the last reading of the culture, after seven days, did not show any hemolysis

The culture of the fungus growing in gelatin at 37 C and kept afterward in a refrigerator did not show any liquefaction. In the incubator at 37 C again, there was liquefaction, and this process continued consistently

*Inoculation of Animals*—Although it will be the subject of another paper I wish to report now that 4 white rats were inoculated intraperitoneally and 1 rabbit



Fig 6—Microscopic appearance of the culture in isotonic solution of sodium chloride. Abundant filamentous forms, some bacilliform (occasionally with one end wider than the other) and others coccoid.  $\times 960$

intravenously with pure culture of the micro-organism in suspension of isotonic solution of sodium chloride and that repeated inoculations in the same animals were made in the same way five times at ten day intervals. I did not observe any positive result in these experimental animals

Four white rats were inoculated subcutaneously with granules taken directly from the lesion on the foot and pulverized and suspended in isotonic solution of sodium chloride. In all these animals a nodule appeared at the site of the injection, the nodules increased slowly in diameter till the twelfth day, in only 1 of these animals the nodule diminished in size and disappeared, in another 2 the nodules opened through the skin and discharged a pasty mass, following which the lesion healed in a week. The microscopic examination of the pasty mass did not reveal any filament and its culture was sterile. In the last one the nodule removed at the end of the second week was taken for microscopic examination

Two rabbits and 4 white rats were inoculated subcutaneously with pure culture in suspension of isotonic solution of sodium chloride, a nodule appeared at the site of the injection, which increased slowly in diameter until the sixth day and remained without any change in the rabbits until the eighth week, when I removed them for microscopic examination, as I shall report in another paper. In the rats the nodules diminished in size and disappeared in the third week, with only one exception, in this animal I removed the nodule at the end of the third week for microscopic examination.

*Treatment*—The etiologic diagnosis of the disease having been established, with the determination of the mycologic species, treatment was initiated with sulfadiazine<sup>6</sup> in doses of 1 Gm every four hours (day and night). After the third week, with the blood sulfadiazine level between 6 and 13 mg per hundred cubic centimeters of blood there was a definite improvement in the patient, with decrease in the size of the foot, in the amount of fluid drainage from the fistulous tracts and in the number of granules, which, having been obtained easily previously, were now obtained with difficulty. After seven and a half weeks, however, it was necessary to stop the medication (212 Gm of sulfadiazine were given) because of anorexia, insomnia, nausea and vomiting and because of an itchy and scaly erythematous dermatosis in plaques located on the face and anterior aspect of the thorax. The patient's resistance required a change of therapy, and after seven days' rest from medication I commenced with administration of sodium propionate,<sup>7</sup> obtained from the E. I. Du Pont de Nemours and Company in this city, and prescribed the dosage of 1 Gm every four hours (day and night), increasing it to 2 Gm after four days. After three days, however, it was again necessary to cease medication, not only because of nausea, asthenia, insomnia and anorexia but also because of the increased volume of the leg and secretion from the fistulous tracts, opening again.

I was unable to convince the patient that he should rest a few days and repeat the sulfonamide treatment in shorter series. He asked to be discharged from the hospital at this time.

#### COMMENT

In conjunction with the records of this hospital and Gorgas Hospital, in the Canal Zone, a review shows that since 1922 in 2 cases Madura foot has been diagnosed, with laboratory confirmation. The ages of the patients were 42 and 43 years respectively. Both were farmers, acquired the infection on the Isthmus of Panama, gave a history of having been traumatized previously in the same foot in which the dis-

6 Gonzalez Ochoa, A., and Zozaya J. Influencia de la sulfanilamida "in vitro" sobre el desarrollo y estructura de *Microsporium canis*, *Sporotrichum schenckii* y *Actinomyces asteroides*, Rev d Inst salub y enferm trop **3** 145 (June) 1942. Keeney, E. L., Ajello L., and Lankford E. Studies on Common Pathogenic Fungi and on *Actinomyces Bovis*. II. In Vitro Effect of Sulfonamides, Bull Johns Hopkins Hosp **75** 393 (Dec) 1944. Peters<sup>31</sup>

7 Gonzalez Ochoa, A., and Ruiloba, J. Accion del propionato de sodio "in vitro" sobre *Actinomyces mexicanus* y *Cephalosporium* sp., ensayo terapeutico en micetomas producidos por estos hongos, Rev d Inst salub y enferm trop **5** 83 (June) 1944. Kenev, E. L., Ajello, L., and Lankford, E. Studies on Common Pathogenic Fungi and on *Actinomyces Bovis*. I. In Vitro Effect of Fatty-Acids, Bull Johns Hopkins Hosp **75** 377 (Dec) 1944.

ease developed afterward and had the lesions localized in the lower left extremity. One was born in Barbados and the other one in the Republic of Panama (province of Chiriquí). One was a Negro, and the other one was a white person.

The macroscopic appearance of the feet in the 2 cases was the classic picture of Madura foot, with its sinus tracts draining almost constantly, malformation of the foot, with impossibility of walking or standing on the foot, odor and similar characteristics, such as were described in India by Gill (1842) and by Vandyke Carter (1860), furthermore, it showed that there was no clinical difference between the forms encountered here and the cases reported in Mexico,<sup>4</sup> Puerto Rico,<sup>1</sup> Cuba,<sup>2</sup> and the southern part of the United States.<sup>3</sup>

Study of the fungus in the first patient, for whom the diagnosis was confirmed (according to the pathologic report by Dr W. C. Cox, of the Gorgas Board of Health, who examined the foot and inferior third of the leg after amputation), revealed aerobic, thick and filamentous forms, generally septated and branching, which produced chlamydospores in culture. Examination of the purulent material from the fistulas never revealed filaments, but spores were observed, which aided in the etiologic diagnosis. Neither in the pus nor in the histopathologic preparations were any characteristic actinomycotic granules or ray fungus observed. From the previous data the diagnosis of Madura foot was made, and the type of fungus present was determined as being of the family Streptomycetaceae.

Study of the fungus of the second patient revealed an aerobic strain with fine filamentous formation, branching and a hyalin-like membrane which was nearly imperceptible, unsegmented and broke readily, forming small masses of bacilli and cocci (a few large spores, of 3 to 4 microns in diameter, were encountered) gram-positive and not acid fast, chlamydospores were not formed. Cultures of the fungus developed an odor resembling that of damp earth. In the purulent exudate, as well as in the biopsy preparation, were observed characteristic granules and ray fungus. Also, in the tissue examined at biopsy there were filaments (which stained red in some slides and blue in others), without "club" formation,<sup>8</sup> but surrounded by a fibrous ring and abundant leukocytic infiltration (especially polymorphonuclear) outside the periphery.

A study of these strains necessary to establish the difference between the two strains leads to the conclusion that the first type, according to the modern concepts of Waksman and Henrici,<sup>9</sup> belonged to the

8 Kessel, J. F., and Golden, E. B. A Comparison of Strains of *Actinomyces* Recovered from Human Lesions, *Am J Trop Med* **18** 689 (Nov) 1938.

9 Waksman, S. A., and Henrici, A. T. The nomenclature and Classification of the Actinomycetes, *J Bact* **46** 337 (Oct) 1943.

family Streptomycetaceae Waksman and Henrici (without establishment of its genus or species), the second type corresponded to the family Actinomycetaceae Buchanan, genus *Nocardia* Trevisan, species *Nocardia asteroides* (Eppinger) Blanchard<sup>10</sup>

The classification of Chalmers and Archibald,<sup>11</sup> classic and useful regardless of the newer ones is still retained, however, with the belief that the distinct types of pathogenic fungi recognized as etiologic agents of Kaempfer's disease (1712) or Madura foot of Colebrook (1846) or mycetoma of Vandyke Carter (1860)<sup>12</sup> by their microscopic appearance may be placed in one of the two groups called actinomycosis and maduromycosis. In accordance with this concept, each of our 2 cases corresponds to one of the mentioned groups: the case of Dr Cox corresponds to maduromycosis (mycetoma) and my case to actinomycosis.

Inoculations were made successively in rabbits and white rats from pure culture in suspension of isotonic solution of sodium chloride and from granules pulverized in suspension of isotonic solution of sodium chloride (intravenously in the rabbits, intraperitoneally in the white rats) without producing the disease. The subcutaneous inoculation of pulverized granules in isotonic solution of sodium chloride in white rats gave rise to nodules, some of which opened spontaneously, another one diminished in size and disappeared, in the only one removed for microscopic examination it was impossible to isolate the same inoculated organism. The subcutaneous inoculation of pure culture in suspension of isotonic solution of sodium chloride in 2 rabbits and 4 white rats gave rise to formation of nodules in each animal, at the end of the eighth week I removed the nodules in the rabbits, in the white rats the nodules diminished in size and disappeared in the third week with only one exception, the nodule of this animal was removed at the end of the third week for microscopic examination, as I shall report in another paper.

The insistence of the patient to be treated medically showed that sulfadiazine,<sup>6</sup> regardless of the age of the disease and the stage of advancement of the lesions, gave the best results, this leaves the impression that if the treatment can be initiated early in the disease the possibilities of cure should be better and the prognosis under these conditions should not be so hopeless as it was in the past. Suspension of treatment because of resistance and sensitization was necessary, and further treatment was refused by the patient. The use of sodium pro-

10 Binford C H and Lane, J D. Actinomyces Due to *Nocardia Asteroides*, *Am J Clin Path* **15** 17 (Jan) 1945

11 Chalmers A J and Archibald, R G. A Sudanese Maduromycosis, *Ann. Trop. Med* **10** 169 (Sept) 1916

12 Castellani A, and Chalmers A J. *Manual of Tropical Medicine*, ed 3, New York: William Wood & Company, 1919, pp 967 and 2110

prionate<sup>7</sup> had to be stopped almost immediately because of the patient's being unable to tolerate it, with an exacerbation of local symptoms resulting

#### SUMMARY

The existence of Madura foot (mycetoma) on the Isthmus of Panama is reported for the first time

It is certain that the condition in the first case corresponded to the known type called maduromycosis (mycetoma) (Streptomycetaceae Waksman and Henrici) and the second to the type actinomycosis (Actinomycetaceae Buchanan). I am unable to indicate the genus or species of the first one because the data at hand are incomplete. The fungus recovered in the second case corresponded to the genus *Nocardia* Trevisan and to the species *Nocardia asteroides* (Eppinger) Blanchard.

The treatment was of a medical nature in spite of the advanced state of the lesion. I feel sure that in early and localized lesions the use of sulfonamide drugs (I used sulfadiazine) not only will prevent the progress of the same but also will cure the infection, because in my case there was definite improvement. I also noted that the use of sodium propionate not only produced an intolerance but also aggravated the local symptoms, necessitating the immediate withdrawal of this medicament.

Dr J. M. Nuñez, Chief of the Medical Department of Hospital Santo Tomas, and Dr H. C. Clark, director of the Gorgas Memorial, gave me suggestions and laboratory privileges. Dr M. Warner cooperated in translating this report.

# PEMPHIGUS VULGARIS

## A Study of the Blood Picture

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**C**LINICAL and laboratory studies have led me to believe that pemphigus vulgaris is a generalized infection<sup>1</sup>. Evidence to support this belief was sought by an examination of the blood picture and is presented in this paper.

Generalized infections produce qualitative and quantitative alterations in the blood picture, which include (a) leukocytosis, which is generally due to an increase in the number of cells of the polymorphonuclear series, (b) changes in the polymorphonuclear leukocytes (these include an increase in the proportion of immature and a corresponding decrease in that of the mature cells, the severer the degree of infection or toxemia resulting from infection, the higher is the proportion of immature cells, in this paper the term "immature" is used to designate the polymorphonuclear leukocytes in which the nucleus is indented but not segmented and also Schilling's staff forms with unsegmented nuclei, which may be in the shape of a T, U or V, all segmented polymorphonuclear leukocytes whose nuclei contain two or more lobes have been regarded as mature cells, illustrations of immature cells are given in figures 7 and 8 of plate III and of mature cells in figures 9, 10 and 11 of the same plate of Wintrobe's "Clinical Hematology"<sup>2</sup>, additional diagrammatic information on these cells is also to be found in figure 28 of that work<sup>3</sup>), (c) decrease in number of eosinophils, with increasing severity of infec-

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1 (a) Grace, A. W. Pemphigus. Effect of Pemphigus Serum on the Leukocytic Picture of Rabbits, *Arch. Dermat. & Syph.* **29** 885 (June) 1934, (b) Pemphigus. Evidence in Support of a Bacteremia as an Explanation of Certain Terminal Changes in the Blood Picture, *ibid.* **30** 22 (July) 1934. (c) Grace, A. W., and Suskind, F. H. An Agent, Transmissible to Mice, Obtained During a Study of Pemphigus Vulgaris, *Proc. Soc. Exper. Biol. & Med.* **37** 324, 1937. (d) Grace, A. W. Pemphigus, *M. Clin. North America* **22** 1345 1938. (e) Grace, A. W. and Suskind, F. H. An Investigation of the Etiology of Pemphigus Vulgaris, *J. Invest. Dermat.* **2** 1, 1939.

2 Wintrobe, M. M. *Clinical Hematology*. Philadelphia, Lea & Febiger, 1942, p. 98.

3 Wintrobe,<sup>2</sup> p. 123.

tion and vice versa, (*d*) reduction in number of lymphocytes,<sup>4</sup> and (*e*) simple chronic anemia, occasioned by defective formation of blood rather than by excessive loss or destruction of blood. In such an anemia there is generally a parallel decrease in the number of corpuscles, the quantity of hemoglobin and the volume of packed cells without change in either the size or the hemoglobin content of the cells.

The normal figures for the blood picture are, as given by Wintrobe<sup>5</sup>

Red blood cells	Men	5,400,000 $\pm$ 800,000 per cubic millimeter
	Women	4,800,000 $\pm$ 600,000 per cubic millimeter
Hemoglobin	Men	16.0 $\pm$ 2.0 Gm per hundred cubic centimeters
	Women	14.0 $\pm$ 2.0 Gm per hundred cubic centimeters
White blood cells		5,000 to 10,000 per cubic millimeter

The normal differential white cell count in adults<sup>6</sup> is as follows: myelocytes 0 per cent, unsegmented polymorphonuclear leukocytes 3 to 5 per cent, segmented polymorphonuclear leukocytes 54 to 62 per cent, lymphocytes 25 to 33 per cent, monocytes 3 to 7 per cent, eosinophils 1 to 3 per cent and basophils 0 to 0.75 per cent.

#### MATERIALS AND METHODS

The studies reported in this paper were carried out on 11 persons, 10 of whom died from pemphigus vulgaris in the New York Hospital after continuous periods of hospitalization, which ranged from twelve to one hundred and seventy-six days. The eleventh person was studied only from the aspect of pruritus and eosinophilia in pemphigus vulgaris. He was under continuous observation for sixty-one days at the Long Island College Hospital, from which he was discharged, to die within six months at Kings County Hospital. The oldest was 68 and the youngest 24 years of age. The average age was 47 years, and there were equal numbers of men and women. Nine persons were Jewish, 1 was a Gentile and the other a Negro. The duration of the disease among the group varied from three months to four years. The progress of all, with the exception of 2, was steadily downhill after admission. In the case of the 2 exceptional persons, who were hospitalized for one hundred and seventy-six and one hundred and four days respectively, definite clinical improvement occurred, and it continued for many weeks. It was manifested by a reduction in the temperature and in the number of lesions and an increased sense of well-being, the degree of betterment, however, was insufficient to warrant discharge from hospital. Complete remission had occurred in 4 persons prior to admission to the hospital and had lasted in 1 case for as long as six months.

It is clear that the persons whose examinations are reported here were in the terminal stages of the disease. It was for that reason that they were chosen, for it was felt that, at that point of the illness, there would be fewer factors influencing the action of the etiologic agent on the blood picture. Such factors as remained, however, were considered from this aspect and included clinical remission and relapse, impending death, increase of body temperature and administration of sulfanilamide.

4 Pinev, A. Recent Advances in Haematology, ed. 3 Philadelphia, P. Blakiston's Son & Co. 1931, p. 143.

5 Wintrobe,<sup>2</sup> p. 72.

6 Wintrobe<sup>2</sup> p. 125.

The examination of the blood was either performed or supervised by the technician of the Hematological Department of the New York Hospital, in the case of the eleventh person the work was carried out at the Long Island College Hospital

#### TOTAL WHITE CELL COUNT

Determinations of the total white cell count were made at one to six day intervals in 9 persons, 6 of whom were also studied from the point of view of red cell count and hemoglobin content. One hundred and seventy-eight counts were made, with an average of 17,410 leukocytes per cubic millimeter, the lowest average reading in any person was 10,910 and the highest 35,600. Consideration of the count in the patients showed that a maximum figure of 48,000 was reached in 1, of between 30,000 and 40,000 in 4, of between 20,000 and 30,000 in 2, and of between 10,000 and 20,000 in 2. Minimum counts ranged from 5,350 to 14,300. The highest point was generally attained during the last weeks or days of life. Thus, it occurred in 5 persons in the last five days and in 2 others in the third week before death. In 1 person, although the maximum figure was found over three months before the end, the count during the last month of life was consistently higher than that of any similar interval of his one hundred and seventy-five day period of continuous observation. In the case of the ninth person the final determination was made too long before death to be considered in this connection. Unlike the results in the case of the red cell count, there were only 2 instances in which the final white cell count was the lowest to be reached, in 3 of the remaining 5 it was above the average for the particular person.

The effect of change in the clinical condition on the total white cell count was studied in the same 2 persons and at the same time as were employed for a similar investigation of the red cell count and hemoglobin content. In view of the fact that the highest white cell count is generally to be found in the final weeks of life, the figures for the period of the relapse which terminated in death were not included in this study, on the grounds not only that they would increase unfairly the count during deterioration but also that they could not be compared with the findings in a subsequent remission. In both persons there was a definite increase in the total white cell count as the clinical condition became worse, in 1 instance the figure rose from an average of 19,630 in improvement to 25,550 in deterioration and in the other from 16,750 to 23,670.

In 10 persons a relation was sought between the body temperature and the white cell count by taking the rectal temperature at the time that blood was withdrawn for the count. One hundred and seventy-eight temperature readings were made, with a maximum, mean and minimum of 104 F, 100.3 F and 97.4 F respectively. The mean tem-

perature may appear low for a group of persons in the final stage of a disease which is due to a virus whose effects are generally lethal for human beings. Temperature above 103 F is, however, unusual in pemphigus vulgaris, less than 4 per cent of the thermometer readings in our series were above that figure, and none was encountered higher than 104 F. The average white cell count was calculated for each of eight levels of temperature, which began at 97 F and increased by 1 F at each level to a maximum of 104 F. With the exception of the levels 98.0 F to 98.9 F and 104.0 F to 104.9 F the deviation of the white cell count, at any level, from the average for all patients at all temperatures (17,410 cells) was less than 1,000 cells. In the two exceptional instances the count exceeded the average by approximately 3,000 and 4,000 cells respectively.

The effect of sulfanilamide on the white cell count was studied in 1 person, in a temporary state of remission, who received 42.3 Gm. of the drug in nine days. The concentration of total sulfanilamide at the end of that period was in the blood serum 13.33 mg. and in the blister fluid 11.76 mg. per hundred cubic centimeters. The fluctuation in the white cell count during the administration of the drug was too great to enable a definite trend to be detected in the number of cells, but the average daily count for the first half of the treatment period 23,280 leukocytes was 23 per cent higher than that for the second half. This difference may have been due either to the depressant action of the sulfanilamide on production of leukocytes or to its bacteriostatic effect on the cutaneous organisms which begin to invade the blisters of pemphigus in numbers sufficient to be detected on culture about eighteen hours after the appearance of these lesions. In the case under observation, the high concentration of the drug in the blister fluid enabled the latter to remain bacteriologically sterile in the unbroken bullae for at least forty-eight hours.

#### POLYMORPHONUCLEAR LEUKOCYTES (NEUTROPHILS)

Observations on the relative proportion of polymorphonuclear leukocytes in the differential white cell count were made at one to six day intervals in 8 persons. One hundred and seventy-one counts were made with average percentages of total, mature and immature neutrophils of 66.9, 30.9 and 36.0 respectively. The lowest and highest average readings in any person were for the total 47.6 and 75.6, for the mature 7.2 and 40.9 and for the immature 24.7 and 55.1 per cent respectively. The lowest and highest single readings were for the total 31.3 and 86.5, for the mature 0.0 and 70.4 and for the immature 6.2 and 82.1 per cent respectively.

The effect of remission and relapse on the relative distribution of mature and immature cells was observed in 2 persons. In the case of the first, during a period of remission of forty-two days the average propor-

tion of mature polymorphonuclear leukocytes accounted for 48.1 and of immature cells for 18.7 per cent of the total number of leukocytes, in one hundred and twenty-eight days of relapse the proportions of these cells were 37.5 and 27.2 per cent respectively. Corresponding figures for the second person were as follows. In a remission of thirty days mature and immature cells comprised 43.8 and 31.3 per cent, and in a relapse of twelve days they comprised 15.6 and 58.1 per cent respectively.

The effect of impending death on the polymorphonuclear leukocytes was studied in 3 persons whose clinical progress was steadily downhill from the day of admission to the hospital until death and whose duration of hospitalization was sufficiently long to enable a satisfactory comparison to be made of the blood cell count in the first and second halves of the period in the hospital. As the end of the second half was occasioned by the death of the patient it is obvious that the clinical condition in this half of the illness was worse than in the first. In the case of 1 person hospitalized for forty days, the proportions of mature and immature cells were 37.3 and 30.7 per cent respectively during the former half and 11.6 and 45.1 per cent during the latter. Corresponding figures for the second person were as follows. In the former half of a period of hospitalization of thirty-four days mature and immature cells comprised 13.5 and 47.9 per cent, and in the latter half they comprised 1.4 and 61.8 per cent respectively. For the third person, hospitalized for twenty days, the figures for the mature and immature cells were for the former half 31.3 and 44.7 per cent and for the latter 21.2 and 60.0 per cent respectively. The influence of impending death on the proportions of mature and immature polymorphonuclear leukocytes was also noted in 2 other persons, whose periods of observation before death were fourteen and twelve days respectively. The percentage of mature cells fell in the first person from 40.4 to 28.3 and in the second from 38.0 to 26.9. The proportion of immature cells correspondingly rose in the first person from 24.3 to 39.2 and in the second from 29.6 to 40.4 per cent. Death followed the last observation in each person at intervals of ten and five days respectively. Counts were also made in 4 persons within two days of death and on the last day itself. In these the proportion of mature cells ranged from 0 to 16 and of immature from 41 to 69 per cent, and the combined totals of mature and immature polymorphonuclear cells were 81, 62, 69 and 54 per cent respectively.

In order to determine the extent to which the proportion of polymorphonuclear leukocytes was influenced by the presence of bacterial microorganisms in the bullous fluid, 1 person, in a temporary state of remission, received 42.3 Gm. of sulfanilamide in nine days. The concentration of total sulfanilamide at the end of that period was in the blood serum 13.33 mg. and in the blister fluid 11.76 mg. per hundred cubic centi-

meters Daily differential white cell counts during the period of treatment and the subsequent nine days revealed the average proportion of mature cells to be 32.7 and 52.3 and of immature forms to be 45.0 and 22.0 per cent for those periods respectively

#### EOSINOPHILS

Consideration of eosinophilia in pemphigus vulgaris was made in 8 persons, 7 of whom were observed for periods ranging from one hundred and four to twelve days before death. The eighth person was included in this study solely in virtue of the severe pruritus of the scalp which accompanied a generalized eruption of pemphigus. After the first twenty-three days of hospitalization the pruritus disappeared, but the patient was retained in the hospital for a further period of observation of thirty-eight days. During the stage of pruritus there was an average eosinophilia of 16.7 per cent, with a maximum and minimum of 24.0 and 12.0 per cent respectively. On the disappearance of itching the proportion of eosinophils immediately fell to below 6 per cent and remained there until the patient's discharge from hospital. No other observations were made on this patient.

The maximum degree of eosinophilia occurred at intervals ranging from sixteen to thirty-six days before death and was in 6 nonpruritic persons 4, 6, 9, 9, 11 and 20 per cent. In none of these was there an eosinophilia of more than 6 per cent during the last thirteen days of life, nor did any nonpruritic person attain a level of more than 6 per cent after having once reached a figure of zero.

The effect of clinical remission on eosinophilia was studied in the 2 patients already referred to in this connection. In 1, who was nonpruritic, the eosinophils constituted 4.1 per cent in remission and 2.4 per cent in relapse. The other received, as a therapeutic measure, sixteen subcutaneous and three intravenous injections of an emulsion of mouse brain containing the inactivated RP virus<sup>7</sup>. The first injection was given one hundred and seventy-two and the last eight days before death. Severe attacks of itching coincided with relapse, and death occurred after a series of acute asthmatic attacks. The average percentage of eosinophils was 1.8 during the forty-two days of the first remission, 12.8 during the forty days of the first relapse, 6.5 in the forty-eight days of the second remission and 14.0 during the thirty-six days of the second relapse, which terminated in death.

The influence of impending death on the proportion of eosinophils was observed in 2 persons, who were hospitalized for forty and thirty-five days respectively. For the first the average figure for the first half of the period of hospitalization was 6.0 per cent and for the second,

<sup>7</sup> Grace, A. W. The Etiologic Agent of Pemphigus Vulgaris, Bull. New York Acad. Med. 22: 480 (Sept.) 1946.

which terminated in death, 2.3 per cent, in the latter patient the corresponding figures were 10.5 and 2.8 per cent respectively. It was possible to obtain a count on the day of death in 4 persons. Two showed an eosinophilia of 1 per cent, and in the others these cells were absent.

#### MONOCYTES

Studies were made on 6 persons, in all of whom the proportion of these cells fluctuated considerably and, at times, attained heights much in excess of normal values. The average percentage of monocytes in the persons examined was 4.1, 4.2, 7.0, 10.3, 12.9 and 14.7 respectively and the maximum readings 10, 11, 12, 18, 23 and 32 respectively. The effect of impending death on the proportion of these cells was studied in 2 persons. In 1 the percentage of monocytes in the first half of the period of hospitalization was 10.2 and in the second half, which terminated in death, was 15.4. The corresponding figures for the other person were 13.5 and 7.0 per cent respectively. Clinical remission and relapse were without effect on the proportion of those cells in the 2 persons studied from this aspect. Sulfanilamide therapy did not produce any significant change in the proportion of the circulating monocytes.

#### LYMPHOCYTES

The proportion of lymphocytes was studied in 9 persons and ranged from 11.4 to 27.4 per cent, the average being 20.1 per cent. There was little difference between the relative distribution of these cells in remission and relapse in 2 persons examined from this aspect. In 1 the figures were 24.8 and 20.4 and in the other 18.2 and 20.4 per cent respectively. In 2 other persons the influence of approaching death on the proportion of lymphocytes was studied. In the first the percentage of these cells in the former half of the period was 18.2 and in the latter 24.8 per cent, the corresponding figures for the second person were 17.4 and 17.2 per cent respectively. Sulfanilamide therapy was without influence on the proportion of circulating lymphocytes.

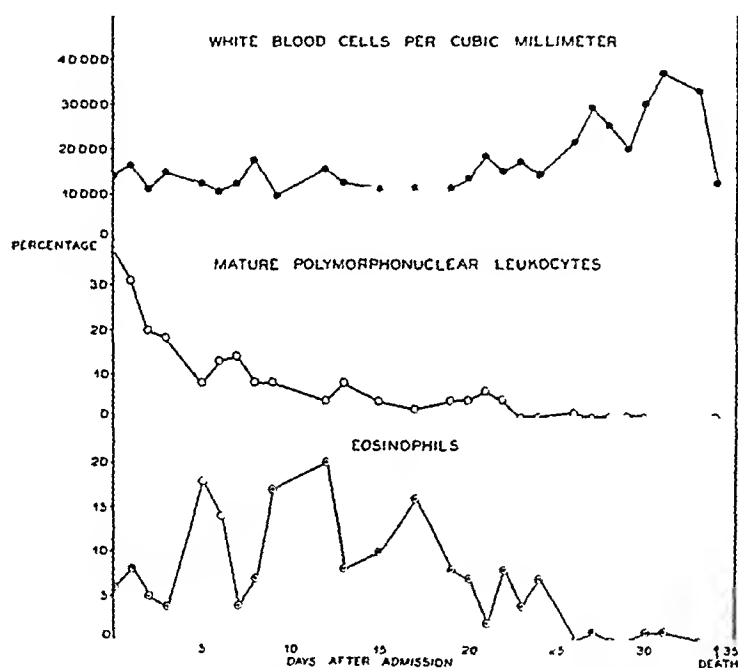
#### BASOPHILS

Basophils were rarely encountered in any person. The average proportion of these cells in one hundred and seventy-seven counts in 10 persons was 0.3 per cent, with a minimum of 0 and a maximum of 3 per cent.

#### RED CELL COUNT AND HEMOGLOBIN CONTENT

Determinations of the red cell count and hemoglobin content were made at intervals ranging from one to eight days in 8 persons. The average of eighty-eight determinations was 3,850,000 for the red cell count and 11.2 Gm. for the hemoglobin content. In 5 persons the highest

figures were found on admission and varied from 3,430,000 to 6,610,000 and 9.6 to 14.9 Gm respectively. Two patients, 1 of whom was hospitalized for one hundred and seventy-six and the other for one hundred and four days, afforded an opportunity to study the effect of clinical improvement on the red cell count and hemoglobin content. In both persons the betterment of the condition was manifested by a reduction in the temperature and in the number of lesions and an increased sense of well-being. The readings in the 2 patients were practically identical and were uninfluenced by the change in the clinical picture. Thus, in 1 case, the cell count and hemoglobin content were 3,850,000 and 11.0 Gm. respectively during improvement and 3,890,000 and 11.5 Gm. in deteri-



Leukocytes, mature neutrophils and eosinophils in peripheral blood of a person in terminal stage of pemphigus vulgaris

oration. The influence of impending death on the determinations was sought in 5 persons in whom the last examinations were made at intervals of two, three, four, ten and twenty-four days respectively before the end. In all, the red cell count and hemoglobin content progressively declined, over an average period of sixteen days, to levels lower than any previously reached in the same person, the final figures ranging from 2,830,000 and 8.8 Gm. to 4,200,000 and 11.3 Gm.

#### COMMENT

In the terminal stages of pemphigus vulgaris many of the elements of the blood picture are affected. The most striking departure from normal occurs in the total white cell count and in the relative proportion of mature and immature polymorphonuclear leukocytes. There is a well

marked and constant leukocytosis, whose maximum is attained during the last days or weeks of life. The degree of leukocytosis is more readily influenced by changes in the general condition of the patient than is the cutaneous picture, and its fluctuation can be employed as an index of the trend of the disease. As, however, the leukocytosis is occasioned both by the etiologic agent of pemphigus and, to a less extent, by the presence of bacterial micro-organisms in the bullous and open lesions of the skin, it can be employed for this purpose only when the patient is under treatment with a bacteriostatic agent. The body temperature is, as a rule, elevated only to a moderate degree, and changes in the clinical condition are not reflected in changes in the temperature chart, death may occur with or without fever. The degree of leukocytosis is independent of the level of body temperature over the range of 97 F to 104 F.

The most sensitive index of change in the general condition of the patient is the proportion of immature polymorphonuclear leukocytes in the peripheral blood. As the presence of bacterial micro-organisms in the cutaneous lesions contributes to their number, the immature polymorphonuclear leukocyte count can be employed for this purpose only when the patient is under treatment with a bacteriostatic agent. With improvement in the clinical condition there is a decrease in the percentage of the immature cells and with deterioration an increase, which may reach such a height that no mature cells can be found at death. As the relative proportion of polymorphonuclear leukocytes—the sum of the immature and mature cells—is within normal range in pemphigus vulgaris, an increase in the immature is accompanied with a decrease in the mature cells.

According to Wintrobe,<sup>8</sup> the highest and most constant eosinophilia (10 to 60 per cent) has been observed in pemphigus and dermatitis herpetiformis. It is likely that the cause of the eosinophilia is not the same in these two diseases. Dermatitis herpetiformis has few systemic manifestations, is seldom debilitating and rarely, if ever, fatal and presents a cutaneous picture characterized chiefly by the development of clusters of small vesicles. The intense pruritus associated with the vesicles leads to their decapitation by scratching soon after their appearance. The reparative powers of the skin in dermatitis herpetiformis, however, are such that healing of individual lesions soon occurs. In this disease, then, the eosinophilia is probably associated with the pruritus and consequent scratching, which introduce the patient's own plasma proteins into his skin. In this connection, I have recently observed an attack of typical urticaria following the second intramuscular injection of human immune globulin in a person convalescing from pemphigus vulgaris, who had received the first injection one week

earlier In contradistinction to dermatitis herpetiformis, pemphigus vulgaris is a systemic disease of high mortality in which the skin presents large and small blisters, crusted and vegetating lesions Pruritus is infrequent and moderate in degree Owing to the weak powers of recuperation of the skin in this disease, individual cutaneous lesions persist for long periods, becoming grossly contaminated and malodorous The presence of such lesions affords an adequate explanation for the occurrence of eosinophilia in pemphigus vulgaris, as it is known that these cells increase in number during the decomposition of body protein<sup>9</sup> As such decomposition in pemphigus probably begins in the bullae, it would be reasonable to expect to find a massing of eosinophils in association with these lesions This has actually been found to occur The bullous fluid when bacteriologically sterile contains a number of leukocytes, of which the eosinophil is frequently the preponderant cell, constituting at times over 80 per cent of the white cells and occurring in a considerably higher proportion than in the circulating blood<sup>10</sup>

The proportion of eosinophils diminishes with deterioration of the general condition, and when a nonpruritic patient becomes sufficiently debilitated the eosinophil count may fall to zero, after which it does not rise again above normal limits In the last two weeks of life the eosinophils do not exceed 6 per cent and are usually less, on the day of death they are few or absent

The terminal stages of pemphigus are associated with a relative and, at times, considerable monocytosis This increase is probably a reflection of the role of the monocyte as a scavenger of particulate materials and bacteria<sup>11</sup> Proof exists<sup>1b</sup> that bacteria enter the circulation from the cutaneous lesions It is, therefore, likely that particulate matter of microscopic size will also find its way into the blood stream through the base of granulation tissue of the lesions

No relation exists between the degree of increase of monocytes and clinical remission or relapse, the presence of impending death or the administration of sulfanilamide Monocytosis is, therefore, an even less sensitive index of the general condition in pemphigus vulgaris than is eosinophilia

The relative proportion of lymphocytes is diminished to a moderate degree and is unaffected by changes in the clinical picture, there is also no observable effect on the basophil leukocytes

The red cell count is diminished in pemphigus vulgaris, with a corresponding reduction in the hemoglobin content Improvement in the general condition, within the limits described in the paper, is without

9 Wintrobe,<sup>2</sup> p 116

10 Grace, A W The Significance of Eosinophilia in Blister Fluid and Peripheral Blood in Pemphigus Vulgaris, to be published

11 Wintrobe<sup>2</sup> p 117

effect on the count and the hemoglobin content. During the last two weeks of life there is a progressive decline in both of these factors to levels lower than any previously reached in the same patient.

In conclusion, the blood picture in pemphigus vulgaris is practically identical with that of a generalized infection. Leukocytosis in this disease, however, does not arise from an increase in the cells of the polymorphonuclear series, it is produced by an increase in the total number of each type of leukocyte present normally in the circulating blood. The absence of neutrophilia may be accounted for on the grounds that the virus of pemphigus,<sup>7</sup> in common with most viruses, is not a pyogenic agent.

#### SUMMARY

Detailed and repeated studies of the blood picture were made for 11 persons over periods ranging from twelve to one hundred and seventy-six days before death from pemphigus vulgaris. The effect of the following conditions on the picture was noted: clinical remission and relapse, impending death and increase of body temperature and administration of sulfanilamide. The blood picture is practically identical with that of a generalized infection.

An explanation is offered for the occurrence of eosinophilia and monocytosis in pemphigus vulgaris and of eosinophilia in dermatitis herpetiformis.

11 Schermerhorn Street

# NERVE LESIONS OF LEPROSY

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AND

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**T**HIS paper deals with the pathologic and bacteriologic aspects of leprosy as it affects the peripheral nerves

In a paper read by us<sup>1</sup> before the Section on Dermatology and Syphilology at the Ninety-Third Annual Session of the American Medical Association, June 10, 1942, we presented the arguments in favor of the pathologic classification of the forms of leprosy introduced by the South American dermatologists. This insists on the presence of nerve lesions in almost every case of leprosy, regardless of the clinical type, and on the importance of distinguishing the lepromatous from the tuberculoid type of this disease, especially from the public health and epidemiologic points of view. At that time we had studied the pathologic changes of the cutaneous lesions in a large number of cases of leprosy and found them in general accord with the South American classification into lepromatous, tuberculoid and nonspecific types. We also remarked then that the pathologic changes were identical whether the lesions affected the skin, the nerves or the viscera. The pathologic study of the nerve lesions of leprosy has been undertaken since then and we have now additional proof that the structure of the lesions of the nerves coincides with that of the lesions of the skin.

The lepromatous patients with profuse tuberculous cutaneous manifestations usually show clinical involvement of the nerves of the large trunks such as the ulnar, median and saphenous nerves and others in a moderate degree. However the most remarkable clinical neuritis is found in the tuberculoid type of leprosy, often in conjunction with cutaneous lesions but at times in the form of almost exclusive neural

Read at the Sixty-Sixth Annual Meeting of the American Dermatological Association, Hot Springs, Va., June 10, 1946

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1 Pardo-Castello, V, and Tiant F R. Leprosy. The Correlation of Its Clinical, Pathologic, Immunologic and Bacteriologic Aspects. J A M A **121** 1264 (April 17) 1943

manifestations, showing enlarged terminal nerves, enormously thickened nerve trunks and areas of cutaneous anesthesia without change in the color or the structure of the skin, although often causing muscular atrophies. These are the cases which were classified under the caption of "neural leprosy" by the International Congress of Leprosy held in Cairo, Egypt,<sup>2</sup> and which, we propose to demonstrate, should be considered as tuberculoid leprosy with predominant location in the peripheral nerves.

We chose for our studies the ulnar nerves of lepromatous patients and the ulnar as well as the superficial branches of the median nerves of patients with the so-called neural types of leprosy. Some of the latter also had cutaneous lesions of the maculopapuloid and annular leprids as well as muscular atrophies, reabsorption of the terminal phalanges and mal perforans plantaris.



Fig 1—Chronic neuritis of the ulnar and antibrachial nerves in a case of tuberculoid leprosy (so-called neural leprosy)

#### THE LEPROMATOUS NERVE LESIONS

Sections made of the ulnar nerves in cases of this type of leprosy with profuse cutaneous lesions showed a structure similar to that of the cutaneous manifestations, the nerves were affected throughout, including the perineural tissues, and the infiltrating cells were those of the histiocytic vacuolar type with apparently empty spaces, similar to those observed in the cells of Virchow. The nerve fibers were degenerated and in many places destroyed, being surrounded by the aforementioned cellular infiltration. Lymphocytes accumulated in the periphery of the groups of vacuolar cells. No fibrosis or scarring was apparent in the sections observed by us. The cellular infiltration in some nerve filaments was in the form of patches of vacuolar cells, while the rest of the nerve tissue seemed little affected.

2 Resolutions and Reports of the International Congress of Leprosy Held in Cairo, J. Egyptian M. A. **21** 138 (March) 1938

Sections of lepromatous nerves stained with *Nachtblau* according to the Hallberg-Reenstierna method<sup>3</sup> showed enormous numbers of Hansen bacilli stained in bright blue, in bundles, stairlike clumps, pairs and singly, among the nerve fibers, in the perineural tissue and in the vacuolar spaces of the cellular infiltrate. The impression was that the tissue did not react greatly to the large number of germs present.



Fig 2—Chronic neuritis of the femoral cutaneous nerve in a case of tuberculoid leprosy (so-called neural leprosy)

#### THE TUBERCULOID NERVE LESIONS

Sections were made of the superficial nerves in cases in which only nerve thickening existed, without cutaneous manifestations, and also of the ulnar nerve in cases with cutaneous tuberculoid lesions. In the two types the pathologic changes were exactly alike, showing that the cases of so-called pure neural leprosy are in reality cases of tuberculoid

3 Hallberg V. A New Method of Staining Tubercle Bacilli (with a Note by J. Reenstierna on the Use of This Method for Staining Leprosy Bacilli), *Acta med Scandinav* 108:12, 1941.

leprosy affecting the peripheral nerves, with or without coincident cutaneous lesions

The sections showed a miliary arrangement, resembling under small microscopic power the lesions of tuberculosis as found in lupus vulgaris and in some sarcoids. This type was composed of thick infiltrations of lymphocytes and epithelioid cells surrounding large multinucleated cells of the giant type. Staining with the Hallberg-Reenstierna method and with Ziehl-Neelsen stain showed no bacilli. In no case of this type could we find necrosis or caseation, the lesions were the exact counterpart of those found in tuberculoid leprosy located in the cutaneous structures.

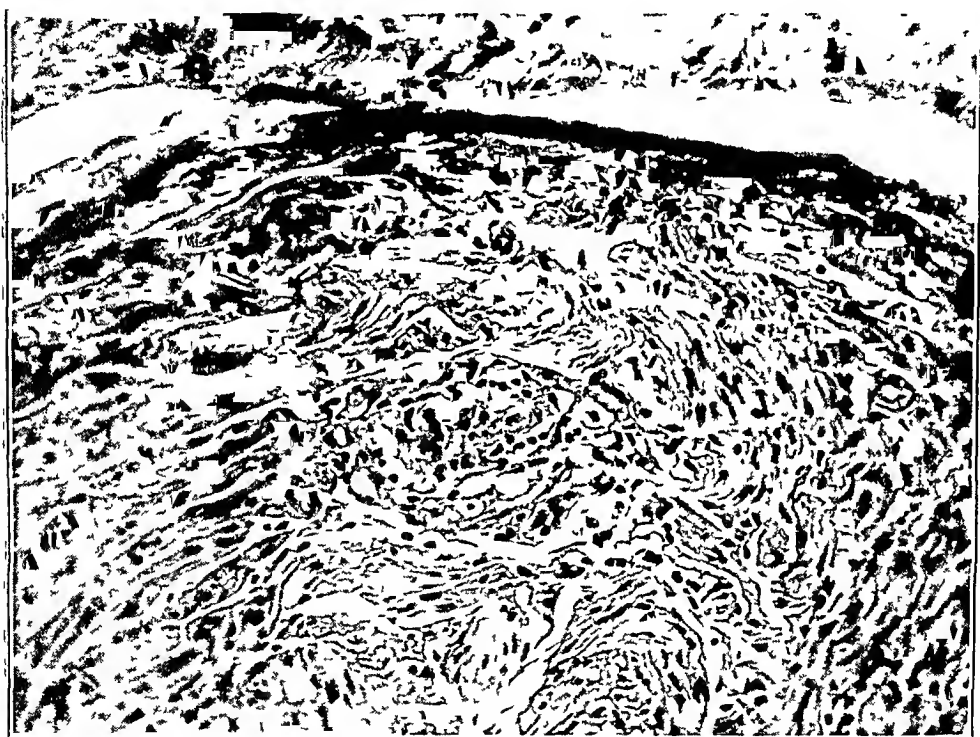


Fig 3—Lepromatous infiltration in a branch of the ulnar nerve in a case of lepromatous leprosy. Notice the large vacuolated cells.

In 2 cases with exclusive involvement of the nerves we found the formation of the so-called nerve abscess, in reality the mass caseation of the tuberculoid manifestations, with complete destruction of the neural tissues. This necrotic material was collected in the center of the nerve and appeared surrounded by a ringlike accumulation of histiocytes, epithelioid cells and lymphocytes with occasional giant cells. In 1 case the necrotic material opened a path to the outside and collected under the skin, resembling an abscess which perforated the skin and emptied itself on the surface. This is the type reported by Rabello, of

Rio de Janeiro,<sup>4</sup> under the name of "colliquative neuritis." In this type we found a few bacilli and some acid-fast granules in the tissue surrounding the necrotic center but none in the necrotic material itself. Nerve scarring and fibrosis were the natural termination of these two types of tuberculoid neuritis.

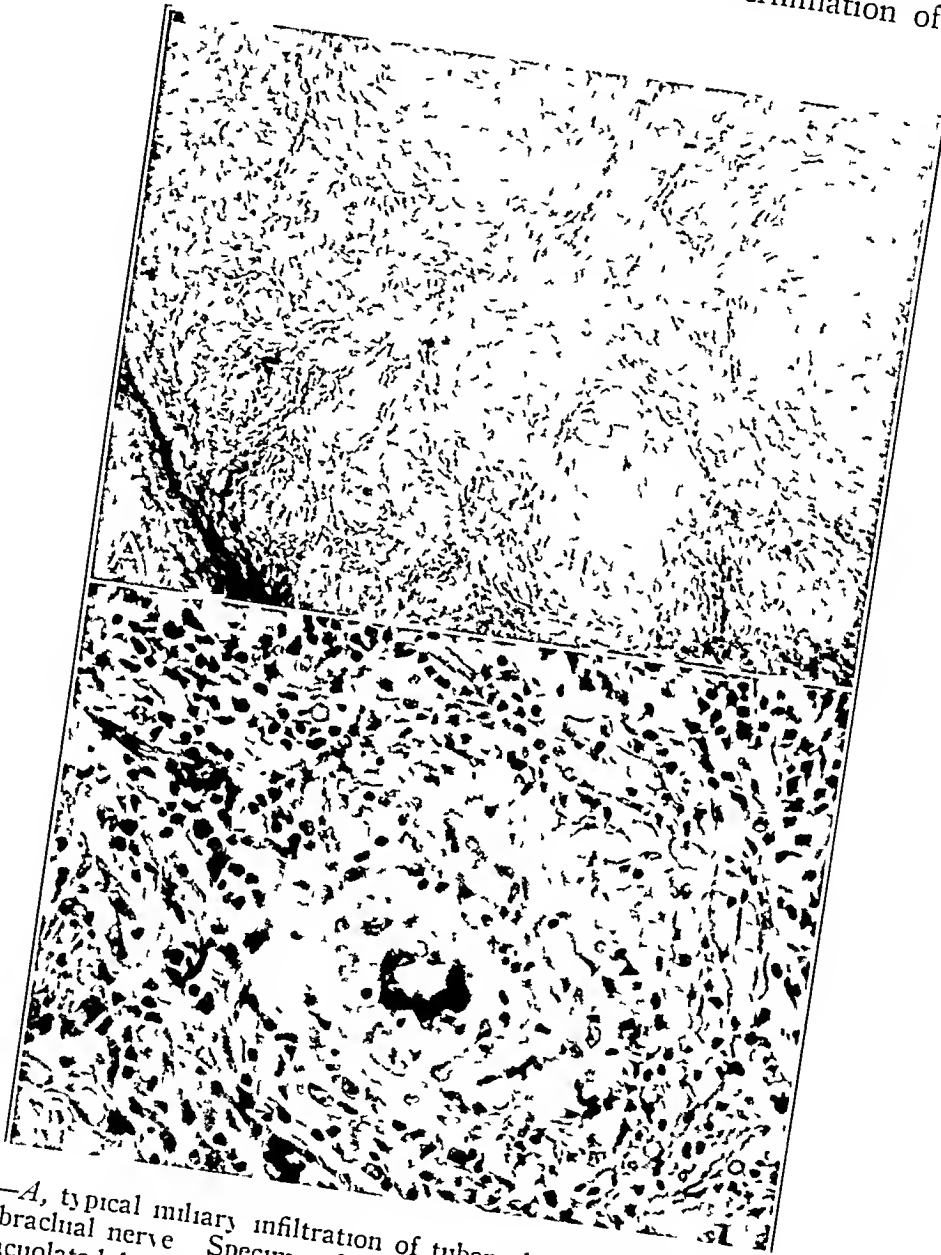


Fig 4—*A*, typical miliary infiltration of tuberculoid leprosy affecting a branch of the antebrachial nerve. Specimen from the patient shown in figure 1. *B*, giant cell and vacuolated histiocytes surrounded by lymphocytes in tuberculoid leprosy of the nerves. Enlargement of the section shown in *A*.

#### SUMMARY AND CONCLUSIONS

1 All patients with leprosy present involvement of the nerves to a greater or lesser degree.

4 Rabello, E, Jr. *Etiologie générale et pathogénie de la lèpre tuberculoïde*, *Rev. brasil. de leprol.* 6: 291 (Sept) 1938.

2 The pathologic study of nerves in cases of the lepromatous type showed the typical structure as observed in the cutaneous manifestations, with accumulations of vacuolar cells and enormous numbers of Hansen bacilli scattered throughout the nerve fibers. There was little tendency to react on the part of the nerve tissue.

3 The pathologic study of enlarged nerves from patients with cutaneous lesions of the tuberculoid type showed structures that could be identified as the counterpart of those found in the skin, consisting of miliary tuberculoid or sarcoid changes and centered with multinucleated giant cells. These lesions end in fibrosis and destruction of the nerves.

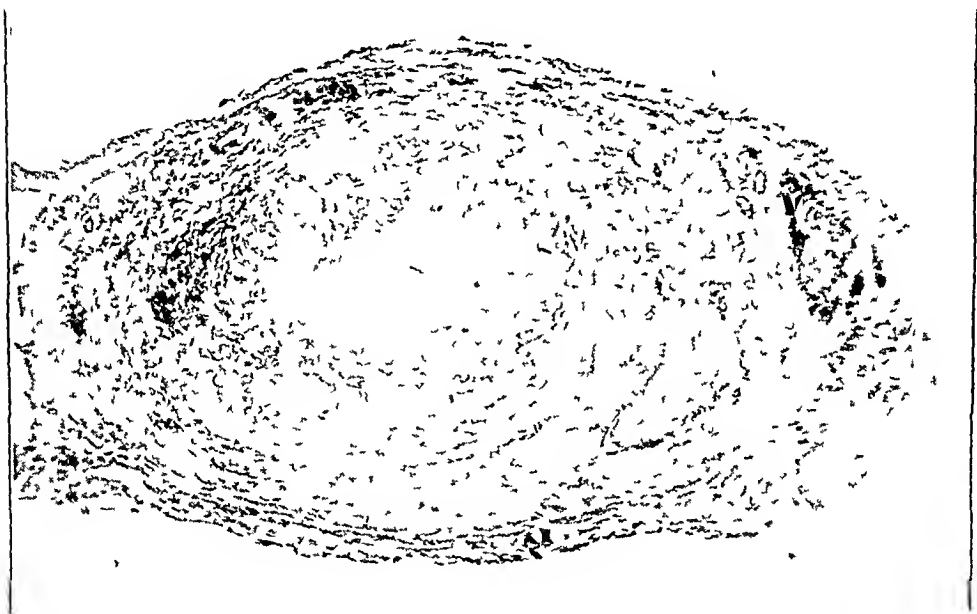


Fig 5—Cross section of a nerve affected with the colliquative type of tuberculoid leprosy, showing central necrosis.

4 The pathologic study of nerves from the patients with thickening of the peripheral nerves, with or without cutaneous lesions, which are considered by those who accept the Cairo classification of the types of leprosy as typical of "neural leprosy," showed also a tuberculoid structure and terminal fibrosis. In some rare cases the process goes on to necrosis, with the formation of caseation collected in the center of the affected nerve or else of a pseudoabscess, which empties itself by adhering to the skin and perforating the cutaneous structures (colliquative neuritis of Rabello). No acid-fast bacilli were demonstrable in these cases except in the inflamed tissues surrounding the necrotic areas; in 1 of our cases, these were found in small numbers and mostly as acid-fast granules.

5 The Hallberg-Reensterna method of staining Hansen bacilli with *Nachtblau* stain was found easy and distinctive, the bacilli showing bright blue

6 In our opinion these studies show that the so-called neural leprosy belongs to the tuberculoid type and corresponds immunologically and bacteriologically to this type as described first by Jadassohn and later by the South American dermatologists. We believe that there is no reason to maintain the existence of "neural" and "cutaneous" forms of leprosy, but these designations may be used to express the location of the lesions, but only with a topographic meaning

#### ABSTRACT OF DISCUSSION

DR BRAULIO SAENZ, Habana, Cuba I wish to congratulate Dr Pardo-Castello on his excellent paper, which is useful for the diagnosis in certain cases of leprosy which may be difficult to recognize, even for those who are acquainted with the various types of this condition. Also, I wish to express my appreciation for the privilege of opening the discussion on this valuable contribution dealing with the nerve lesions observed in leprosy

The picture corresponding to lepromatous leprosy is well known, both clinically and histopathologically, the difficulties arising in cases of so-called neural and tuberculoid leprosy. In these the features are not so well defined, and many points should be carefully considered before one arrives at a definite conclusion. For instance, the responsible etiologic agent of the various granulomatous infections is only rarely demonstrated in the sections, on the other hand, sometimes it may have disappeared, and in other cases it may be produced by the action of the toxins. Then it must be admitted that some other criteria are needed for establishment of a correct diagnosis. The study of the infiltrate in itself does not help either, because it is difficult at times to differentiate the tuberculoid structure of various conditions, such as lupus vulgaris, some sarcoids and mycosis, conditions in which the infiltrate is extremely similar.

It is for this reason that this paper is useful, because it emphasizes the changes early observed in the nerves in all types of leprosy, changes that are detectable not only on the lesions of the skin but also in places of the skin which are supposed to be absolutely normal.

Tuberculoid leprosy was first described by Jadassohn in 1898, but it was not well established as an entity until 1927 by Darier. Since then, many contributions have been made, a few have been made in Europe, but most of the work has been done by Wade, in South Africa, Wade and Rodriguez, in the Philippines, Lowe, in India, and Reiss, in China. In Brazil should be mentioned the papers of Motta, Seminario and Gaviña Alvarado, Grieco and Rabello Jr, and in Argentina the work has been done by Bahiña y Bassombrio, J. M. Fernandez, Schujman and Castañe, these last three men under the direction of the late Dr Enrique Fidanza, who was an honorary member of this association.

At the meeting of this association in 1938, at Del Monte, Calif., I read a paper on tuberculoid leprosy, and at that time I emphasized the necessity of a study of all cases of tuberculoid leprosy from a histologic point of view, mentioning the constant presence of anesthesia or hypesthesia of the lesions, the scarcity or absence of *Mycobacterium leprae*, the positive Mitsuda reaction and the benign course of the disease. As Dr Pardo-Castello stated, the lesions of the nonmyelinated fibers

of the nerves of the upper corium are not easy to detect, because of their simple structure, the changes being more pronounced on the deeper myelinic nerves because they are more differentiated and resistant than the superficial ones of the upper corium. For this reason, the biopsy specimens should be taken deep enough in the subcutaneous tissue in order to study the myelinic fibers, where the changes are more pronounced and lasting.

In regard to the opinion of Dr Pardo-Castello that neural leprosy is a type of tuberculoid leprosy, I do not agree with him, but in my experience I have observed that muscular atrophy in pure neural leprosy is not often seen, as is the rule in the mixed types of the disease. I have followed a score of patients who presented great involvement of the superficial cervical plexus. The nerve branches could be seen protruding under the skin. Nevertheless, these patients did not suffer from the acute neuralgic pains that accompany the neuritis of lepromatous leprosy. The disease, with treatment, regressed and disappeared, the nerve did not show any more enlargement, and, besides, even the anesthesia or hypesthesia regressed and what was left in some cases was a slight numbness.

In addition to the study of the infiltrate in tuberculoid leprosy, so clearly expressed by Dr Pardo-Castello, I think that it is well to mention the opinion of Dr Castañe, of Rosario, Argentina. He said that it is worth while to state that the infiltrate in these cases adopts always a peculiar picture or pattern, that is to say that the initial lesions are observed next to the nerve branches, not near the blood vessels. The infiltrate pushes the blood vessels toward the periphery. This special arrangement he calls para-arterial neural infiltration, which he considers typical of tuberculoid leprosy, affirming that it is present in 74 per cent of all cases that he has studied and stating that it is the best differential diagnosis between tuberculoid leprosy and any other disorder producing tuberculoid infiltration.

I have had no experience with the Hallberg-Reenstierna *nachtblau* staining method for detecting *Mycobacterium leprae*, I have always used Ziehl, Klingmüller and Gallego stains, but I shall be glad to try it in future cases.

DR WILEY M. SAMS, Miami, Fla. I have been close to the problem of leprosy in that I live but a short distance from Cuba and have, in thirteen years, had the opportunity to observe 17 cases, a relatively small number in comparison with those reported in neighboring countries.

My interest is in the problem of early diagnosis, and I am entirely in accord with the South American classification which has been presented. I am interested now in the epidemiology and in the infectious nature of some of the problems that arise in my community. Most of the patients that I have had the opportunity to observe present lesions of the tuberculoid type, with only 2 or 3 showing predominantly lepromatous lesions. I have observed in 1 case the transition from the tuberculoid into the lepromatous type when the patient had a coexisting severe illness. Is it possible that such may occur without regard to the condition manifested or to the patient's immunologic reaction? If persons with tuberculoid lesions who react positively to lepromin would maintain this status permanently, it would simplify many of our problems in handling such cases.

DR NORMAN N. EPSTEIN, San Francisco. I should like to ask Dr Pardo-Castello if he would discuss the value of the cutaneous tests in differentiating types of leprosy.

DR CORNELIUS F. LEHMANN, San Antonio, Texas. Mr Chairman, I am delighted to hear Dr Pardo-Castello, who has had such an extensive study of this subject, clearly define to us and bring out this point that leprosy is not to be

divided into just neural and lepromatous. We read that the lepra bacillus has an affinity to nerve tissue. For a long time I felt that the first tissue that was ever affected was the nerve. When I see a case in which I want to substantiate a diagnosis, the first thing I look for is enlarged nerves or nodulations, and I have had the experience in numerous instances in these tuberculoid types in which I have failed absolutely to detect at first examination any enlargement of nerves or nodulations. I recall 1 patient who presented recurrent leprosy fever. That was later diagnosed as bullous erythema multiforme on numerous occasions, and it was three or four years before nodules developed from which the bacilli could be recovered.

I have had little experience with the histamine and lepromin tests and should like Dr. Pardo-Castello again to bring out the value of that in the early diagnosis. I have had several instances in which the diagnosis was difficult in early cases because the patients presented only two or three lesions that were of the tuberculoid type.

DR. FRED D. WEIDMAN, Philadelphia. I first read of the *nachtblau* method in the Norwegian literature in connection with Schaumann's disease, in which Schaumann himself reported the demonstration of tubercle bacilli in the lymph nodes by the Hallberg technic. Inasmuch as I have not had a chance to use it, I should like to know what his advantage might be over the usual Ziehl-Neelsen technic.

All of us know that Dr. Pardo-Castello has a most extensive acquaintance with leprosy and knows the literature thoroughly, and I should like to ask him why it is that, contrary to the case for the tubercle bacillus, this other acid-fast organism so regularly elects nerve tissue. We think of nerve tissue as a tissue that is particularly rich in lipid substances. Is there anything in the literature to indicate that there is a physicochemical explanation, based on a special kind of lipid content perhaps, or other factors in the leprosy bacillus which determine its selection of nerve tissue?

DR. V. PARDO-CASTELLO, Habana, Cuba. I want to thank you gentlemen for the discussion. The concept of leprosy from the point of view of public health is of the greatest importance, because in the countries where leprosy is endemic, such as in my country and others in South America, it is absolutely impossible, or practically so, to segregate all patients. It would be beyond all possibilities from the economic point of view. It should be about as difficult as to try to segregate all patients with tuberculosis into hospitals or sanatoriums. Therefore, we must find out who are the patients that are really dangerous to the community, those are the patients with lepromatous leprosy. I do not see any reason why the patients with tuberculoid leprosy should be segregated. Those patients must be and should be under sanitary supervision, but there is no reason to raise such a terrific noise about 1 simple case of tuberculoid leprosy affecting the nerves, particularly the case of so-called neural leprosy, for instance.

The importance of lepromin in the prognosis of leprosy is great. Lepromin is not a diagnostic test. That is, many patients with leprosy are lepromin positive, and others are lepromin negative. Those that are lepromin negative are the patients with lepromatous leprosy, all those with the contagious type of the disease and all those without defensive powers are lepromin negative. On the contrary, all the patients with tuberculoid leprosy, those who have adequate defenses, that is, who show few, if any, bacilli in their tissues and none in the secretions are lepromin positive. Therefore, there is a simple test from the point of view of public health to show which patients should be segregated and those that should not.

The simplest test, of course, is to show the presence of Hansen bacilli in the secretions and the tissues, but it is not easy in all cases to demonstrate the presence of these bacilli. Therefore, the lepromin test would be of prognostic value in that a positive reaction would occur in a patient who is probably poor in bacilli and a patient that has adequate defenses, one that has little possibility of transmitting the disease to another human being.

It is easy to perform the lepromin test. It is done just as an intradermal tuberculin test, and the preparation of the antigen is also easy with a lepromatous piece of tissue. I shall not go into the technic because that would take too much time.

As to the histamine test that one of the discussers mentioned, of course that is a diagnostic test of interrupted conduction of the peripheral nerves and applies to any peripheral neuritis that causes destruction of the nerve fibers. It is a fine test to distinguish and to diagnose leprosy in persons who will not cooperate, such as children and persons who refuse to consider their sensations abnormal—persons who are tested for pain sensation or for heat sensation or thermal sensations in general—and refuse to cooperate. We want to remember that there are persons who want to fool the physicians and that there are children and feebleminded or primitive persons who do not understand what the difference between contact and pain means.

In that case the histamine test will give the answer, that is, the histamine will not show the typical triple response of Lewis but will produce a wheal and no surrounding erythema. That shows that there is peripheral neuritis of the destructive type. That, of course, would be true in vitamin B deficiency, it would be true in destruction of the peripheral nerves due to injury. While that might also be true in alcoholic neuritis or arsenical neuritis, the histamine test is useful in leprosy in differentiating from syringomyelia producing similar sensory manifestations of the peripheral parts of the body. In that case, the peripheral nerves are not really affected, that is, the conductivity of the nerves is preserved. Therefore, the histamine would be of value in distinguishing between these two diseases.

Finally, as to the stain, I am indebted to Dr. Weidman for the Hallberg-Reenstierna stain. I did not know where to get the *Nachtblau*, which is a German dye and is off the market now. I think that a substitute in the form of a similar dye is going to be made in this country. It is easy to employ, and it will show the most abundant blue bacilli, both in tuberculosis and in leprosy. We do not have the difficulty of using too much of our acid alcohol and decoloring all our bacilli, as often happens, particularly in leprosy bacilli, which are not so acid fast as the bacillus of tuberculosis.

I do not know, in answer to Dr. Weidman, and I do not think that we have had explained satisfactorily the reason for the preference of the leprosy bacillus for the peripheral nerves. We know that they go up from the skin, and it has been proved to a certain extent that the lesions begin in the skin and the bacilli are carried there by the circulation, then they attack, by preference, the peripheral nerves, the terminations and the nerve endings in the skin and travel in an ascending, centripetal course, without ever arriving, so far as has been shown, at the spinal cord. They reach as far as the roots of the cord but not the cord itself.

# TOPICAL PENICILLIN THERAPY

## II The Principles of Local Therapy with Penicillin Ointment Mixtures

LEON GOLDMAN, M D

RAYMOND R SUSKIND, M D

AND

FORMAN FRIEND, M D

CINCINNATI

### THE PRINCIPLES OF LOCAL THERAPY WITH PENICILLIN OINTMENT MIXTURES

**T**HE EFFECTIVE antimicrobial properties of penicillin make its range of application extensive. Early in the investigative history of this antibiotic its topical action was recognized. Since that time, attempts have been made to employ penicillin in the treatment of numerous diseases of the skin. Because of the many factors involved in the topical application of a relatively unstable chemotherapeutic agent, the use of penicillin in ointment form for cutaneous infections has not been a simple matter. Our own experiences with more than 400 cases, however, show that, when properly prepared and rationally employed, penicillin ointment mixtures are of value in dermatologic therapy.

With penicillin ointments in their present state of development, certain important factors must be considered in their preparation, storing, dispensing and application to insure maximum therapeutic effectiveness.

**1 Preparation** Factors to be considered are (1) stability, (2) dispersion of the penicillin in the proper medium, (3) diffusion from the base, (4) irritation and (5) concentration.

**Stability** Stability depends on the absence of water in the ointment, the use of a relatively stable penicillin salt such as calcium penicillin rather than sodium penicillin and the maintenance of comparative sterility during preparation. The temperature of the mixture during preparation should not exceed 15 C and should be preferably lower. The presumed expiration date should be recorded.

**Dispersion** Since it is imperative that the penicillin come into direct contact with the infectious agent in maximum concentration, the anti-

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Materials for the study were furnished by the Bristol Laboratories Inc., and the Schenley Laboratories Inc. The study was done in part with grants from the Bristol Laboratories, Inc., and the Schenley Laboratories, Inc.

biotic must be dispersed throughout the vehicle in the form of a fine emulsion. Some factors influencing dispersion are consistency, viscosity and thoroughness of mixing.

**Diffusion** Another factor which is responsible for the concentration of penicillin in the tissue fluids is the rate of diffusion of the antibiotic from the base. The base should be so chosen as to allow uniform but not too rapid diffusion into the tissue fluids.

**Irritation** Most of the simple bases used in water-free ointments, such as petrolatum, liquid petrolatum, peanut oil, beeswax, synthetic higher alcohols such as Lanette wax S X and wool fat, are usually not irritating. In a certain, and increasing, percentage (as high as 10 per cent?) of cases penicillin per se may be sensitizing.

**Concentration** A concentration of 500 to 1,000 units of calcium penicillin per gram of ointment is preferable in most cases in which use of penicillin ointment is indicated. In our study we have used concentrations as high as 20,000 units per gram and produced no irritation and only rarely increase in sensitization. Comparative studies employing ointments of different concentrations are still in progress.

**2 Storing** Calcium penicillin in the water-free bases which are now used requires continued refrigeration before and after dispensing, of 15 C or lower. Reputable water-free ointments containing calcium penicillin may not lose potency significantly if kept at room temperature for one or two weeks. In some cases, e g., of impetigo, the application of the ointment is usually maintained for this brief period. Nevertheless, because of variations in the stability of ointments at so-called room temperature and the variation in room temperature conditions, it is advisable to instruct all patients to refrigerate the penicillin ointment prescribed to avoid possible mishaps.

**3 Dispensing and Application**—A metal ointment tube with a small bore nozzle is the container of preference. There is less opportunity for contamination of the ointment in this container than in a glass jar or metal can. Jars must be sterilized, and ointment should be removed with the aid of a sterile applicator or a knife blade which has been previously sterilized by flaming.

The stability of ointments has been determined by assay of ointments for penicillin activity at repeated intervals, the ointments being stored at room and incubation temperatures as well as various refrigeration temperatures. Preliminary studies have also been made by us to determine the duration of activity of the penicillin after the ointment mixture is applied to the skin. Two methods of penicillin ointment assay have been used.

**1 Ether Extraction Method** The penicillin is extracted from the base with ether. The total penicillin extracted from a given weight

of ointment is determined by a serial dilution technic, *Bacillus subtilis* being employed as the indicator organism<sup>1</sup>

**2 Crude Cup Method** The ointment is placed directly in the penicillin assay cups which have been set into staphylococcic-seeded agar mediums. A comparison of the zone of inhibition with those resulting from the standard ointments and solutions determines approximately the activity of the test ointment.

#### SIMPLE TOPICAL THERAPY

Simple topical therapy with penicillin ointment mixtures may be distinguished from combined topical and parenteral therapy. The use of penicillin locally depends on the known fact that there are numerous pathogenic micro-organisms which are primary or secondary invaders of the skin and which are sensitive to penicillin. Susceptibility to penicillin is a relative rather than an absolute characteristic. There are organisms which are highly sensitive to extremely low concentrations of penicillin, and there are many more organisms which are less sensitive but which are inhibited by moderate concentrations. In general, the susceptibility of pathogenic micro-organisms *in vivo* parallels the sensitivity of the organism *in vitro*. Included in this group of sensitive micro-organisms in relationship to common cutaneous infections are *Staphylococcus albus*, *Staphylococcus aureus*, *Streptococcus haemolyticus*, nonhemolytic streptococci, *Diplococcus pneumoniae*, *Corynebacterium diphtheriae* and many others. Theoretically the topical application of penicillin provides a means of placing penicillin in high concentrations in close proximity with the growing sensitive invaders. The amount of penicillin which actually affects the organisms depends on the penetrability of the mixture and the rate of the diffusion of the product from the base. The antibacterial effect of the achieved concentration depends on the duration of contact with the organism. At the present time no adequate method has been worked out to determine the penicillin concentration in the tissue fluid of an infected area of the skin following the application of the antibiotic ointment.

In actual practice considerable knowledge may be obtained through bacteriologic studies of the local lesion and by determining the susceptibility of the isolated organism (s) to penicillin. To determine susceptibility of bacteria the culture of the isolated organism is tested against penicillin concentrations varying from 1 unit per cubic centimeter to 0.0015 unit per cubic centimeter. The fate of the infectious agent may be followed by repeated cultures during the course of the treatment.

1 Randall, W. A., Price, C. W., and Welch, H. Estimation of Penicillin in Body Fluids, *Science* 101: 365, 1945.

Clinical and laboratory studies with penicillin ointment mixtures demonstrate its comparative usefulness in many types of cutaneous diseases

*Conditions for Which Penicillin is Definitely Indicated* 1 Impetigo Results with penicillin ointment mixtures are gratifying. The lesions clear rapidly in both acute and chronic cases. Resistant types of impetigo which do not respond to the usual local chemotherapy will often respond quickly to the antibiotic ointment. The ointment is usually applied once daily or more frequently after scrubs with soap and warm water. Perhaps the frequency of application is related to the concentration of penicillin and the persistency of the ointment on the lesion.

2 Superficial Impetiginized Dermatitis. Examples of superficial impetiginized dermatitis are infected contact dermatitis and scabies. The special problem of infectious eczematoid dermatitis is a different cutaneous reaction and is discussed in another section of this report.

3 Superficial Pustular Folliculitis. Results are satisfactory in cases of superficial pustular folliculitis. When facial lesions are treated with the ointment, the patient should be observed carefully because at times in facial areas, in adults especially, penicillin ointments may be sensitizing. The reason for this has yet to be determined.

4 Dermatophytosis with Secondary Pyogenic Infection. Excellent results have been obtained in the treatment of the secondarily infected interdigital type. The course of the primary fungous infection is not influenced.

5 Superficial Wounds. Penicillin ointment may be used to prevent secondary infection.

6 Operative Sites. Penicillin ointments may be used in preference to penicillin solutions in potentially infected or actually infected areas, e. g., when specimens have been removed for biopsies or when circumcisions have been done.

7 Burns. In pressure dressings ointments are used following debridement to prevent infection.

8 Infected Sinus Tracts and Cyst Cavities. Penicillin ointments are useful in infected sinus tracts and cyst cavities.

9 Aphthous Stomatitis. In cases in which penicillin-sensitive streptococci predominate, topical application of the antibiotic is indicated. Comparative studies with troches or lozenges have not been made.

*Conditions in Which Penicillin is of Possible Benefit*—1 Infectious Eczematoid Dermatitis. There are several complicating factors to be considered in the treatment of this disease with penicillin ointment. Many of the cases reveal the presence of penicillin-resistant organisms.

Also the patients will often not tolerate greases and the condition will become worse with any type of greasy medicament. When this occurs penicillin solution packs may be used.

2 *Pyodermas of the Deeper Type* An example of such a condition is pyoderma gangrenosum. The value of topical therapy is limited to the prevention of contiguity spread of the lesions. Combined parenteral-topical therapy is recommended. When topical therapy is employed and ointments of high concentrations of penicillin are available, 10,000 to 20,000 units per gram may be employed. An experimental study was conducted in which concentrations of 10,000 units per gram and 20,000 units per gram were used in a small group of cases of pyoderma gangrenosum, with some benefit. The investigation in other cases continues.

3 *Ulcers* Serious consideration of all etiologic factors must be given in all such cases. If ulceration is on a simple pyogenic basis, lesions may respond to the ointment alone. Mixed infections with the presence of penicillin-resistant organisms make the problem more complex. In the critical evaluation of penicillin therapy, vascular factors, bacteriology, immunobiology and histopathology of the lesion should be studied. Evaluation of nutritional and cardiac status is frequently indicated.

4 *Infectious Exanthemas* Penicillin ointment may be used to prevent secondary infection with subsequent scarring, as in varicella.

5 *Seborrheic Dermatitis* Satisfactory results have been observed in a few cases, but further investigation is necessary.

6 *Sycosis Barbae* Penicillin ointment is unsatisfactory when used alone. When used along with depilation of infected hairs and roentgen therapy and other forms of adjuvant treatment, the reported results are often good.<sup>2</sup>

Penicillin is of no value for (1) deep infections in which the ointment cannot penetrate the infected area (carbuncles or deep cellulitis), (2) psoriasis, (3) lupus erythematosus, (4) pemphigus, (5) dermatitis herpetiformis, (6) "stasis" eczematoid dermatitis, (7) acne vulgaris (both the papulopustular and the nodulocystic varieties fail to respond), and (8) herpes labialis.

Penicillin is contraindicated (1) in cases in which eczematous penicillin sensitivity is demonstrated, (2) in cases in which the infectious organism is penicillin resistant, (3) when the ointment is nonsterile or inactive (patients should be instructed to notice the expiration date on all commercial penicillin ointments and not accept ointments in which the expiration date has passed), and (4) in cases in which there are contraindications to the use of greases.

2 Cohen, T. M., and Pfaff, R. O. Penicillin in Dermatologic Therapy, *Arch Dermat & Syph* 51:173 (March) 1945.

COMBINED TOPICAL AND PARENTERAL ADMINISTRATION  
OF PENICILLIN

Possible indications for combined topical and parenteral use of penicillin are (1) superficial infections with invasion of the blood stream, (2) secondarily infected virus infections, e g, vaccinia and variola in a case of severe eczema vaccinatum and in a case of Kaposi's varicelliform dermatitis, combined therapy was used to combat widespread staphylococcic infection, in the case of eczema vaccinatum the side of the face to which the ointment was applied cleared much more rapidly than the other, to which no chemotherapeutic agent was applied), and (3) deep pyogenic infections, e g, pyoderma gangrenosum. There is no evidence that combined therapy produced any more toxic reactions than either parenteral or topical therapy alone. There is also some question as to whether topical use of penicillin is necessary when parenteral therapy is being administered. Studies in the future may reveal that parenteral use of penicillin can do all that topical use of penicillin can accomplish. As indicated previously, theoretically, topical use of penicillin should produce higher local concentrations than parenteral administration of penicillin.

Penicillin assays were made in 2 cases of bulla formation in which parenteral administration of penicillin had been used. The bulla fluid in a case of epidermolysis bullosa showed a relatively lower concentration than the serum which was assayed at the same time. In a case of meningococcemia with gangrene of the extremities, the bulla fluid contained no penicillin. This was not surprising, considering the local circulatory disturbances which were present. Not enough work has been done to be able to compare this study with our work on bulla concentrations during sulfonamide therapy.

## OTHER PROBLEMS UNDER INVESTIGATION

Although 500 to 1,000 units of penicillin per gram of ointment is used routinely in the majority of cases, there is no definite information available to prove that this concentration gives maximum results in all cases. We have at present under investigation 68 patients who are being treated with penicillin ointment mixtures with concentrations varying from 5,000 to 20,000 units per gram. This group includes cases of pyoderma gangrenosum, favus, infected sebaceous and pilonidal cysts, ulcers of the legs, impetigo, hidrous adenitis axillaris and infectious eczematoid dermatitis.

Other problems which require further investigation concern penetrability and stability of topical penicillin mixtures. Our attempts to prepare lotions which are as stable as water-free ointments have not been successful. As yet, no studies have been done to determine

whether the type of penicillin, F, X, G or other fractions, is as important in topical as in parenteral therapy

#### TOXIC REACTIONS

Preliminary studies indicate that penicillin is a good sensitizing agent. The reactions which are observed are chiefly cutaneous. These may be produced by either parenteral or topical therapy or both. Cutaneous eruptions following penicillin therapy include dermatitis venenata, urticaria, endogenous vesicular dermatitis of the hands, feet, groin and axilla and maculopapular eruptions. In a previous report we have attempted to evaluate 13 cases of eczematous contact dermatitis in which penicillin ointments were employed. In 12 of the 13 cases the reactions were limited to the face. These were characterized by burning, itching and erythema and in the majority of cases reactions occurred within one to three days after the initial application.

Urticaria occurs following parenteral therapy in about 2 to 5 per cent of patients<sup>3</sup>. It is rarely seen following topical treatment. Its appearance may vary in time from one day after the initiation of therapy to one to three weeks following the discontinuation of therapy. Although with parenteral therapy the appearance of urticaria may be no contraindication to continuation of treatment, in cases which manifest infected cutaneous lesions, an associated urticaria is undesirable and application of penicillin should be stopped.

Erythematous vesicular eruptions of the hands, feet, axillas and groin are usually seen in patients under parenteral treatment.

We have seen several unusual cases of reactions to penicillin. One of the patients was a nurse in whom there developed symptoms of serum sickness when she handled penicillin solutions. Dermatitis from penicillin, cutaneous contact, is occurring more frequently in physicians and nurses. The other was a patient in whom there developed angioneurotic edema limited to the face after a nose spray with penicillin solution. We have observed cheilitis from topical applications and stomatitis from topical and, rarely, from parenteral therapy with penicillin.

#### PENICILLIN MIXTURES

Ointments which incorporate penicillin and other chemotherapeutic agents are being studied. We have employed a mixture of hemin and penicillin for the past year. The rationale for the use of hemin is that this fraction of the hemoglobin complex is reported to stimulate fibroblast proliferation and subsequent epithelization. The conditions treated with hemin-penicillin mixtures included indolent ulcerative lesions

3 Keefer, C. S., and Anderson, D. G. *Penicillin in the Treatment of Infections*, New York, Oxford University Press, 1945, p. 938.

which failed to heal under any other type of therapy, sites of excision of tumors of the skin, sites of biopsy and impetigo

Other chemical bacteriostatic or bactericidal agents which do not affect penicillin in any way may be used to enhance its antimicrobial action in ointment mixtures. The use of chemotherapeutic agents which will inactivate or destroy micro-organisms which are insusceptible to penicillin are especially advantageous.

For the future, mixtures of two antibiotics, as penicillin and streptomycin, would seem to hold great promise. Streptomycin is still relatively unavailable, and its use in ointments will have to await increased production. Penicillin-tyrothricin combinations have also been studied.

#### PENICILLIN FASTNESS AND TOPICAL THERAPY

The influence of topical penicillin therapy in creating penicillin-fast strains of pathogenic micro-organisms is still to be ascertained. The fact that some lesions will show an early rapid response and subsequently remain unchanged despite continued treatment with penicillin only suggests the possibility of penicillin fastness. Lesions may not respond for other reasons. 1. Penicillin-insensitive organisms may be present. 2. Higher concentrations of the antibiotic may be necessary. 3. The ointment may be inactive. 4. Contributory nonbacteriologic factors may be keeping the lesions active.

#### CONCLUSIONS

Properly prepared penicillin ointment mixtures of suitable concentration provide a means of therapy for certain selected superficial dermatoses in which the causative organisms are sensitive to penicillin. In order for penicillin ointment therapy to be effective, definite qualifications must be considered. The mixture must be properly prepared, stored, dispensed and applied in the conditions caused by pathogenic micro-organisms which are inhibited by penicillin.

Deep infections, infections of unknown cause, infections in which the organism is resistant to penicillin and contraindications to the use of grease are some of the conditions in which penicillin ointment mixtures should not be used.

Eczematous contact reactions and other forms of reactions of the skin and mucous membrane are seen following topical penicillin therapy. The frequency and severity of these reactions will determine whether topical penicillin therapy in selected dermatoses is to be discarded in favor of equally effective nonsensitizing agents. Moreover, if it is established that topical penicillin therapy also sensitizes a person so that adequate parenteral penicillin therapy cannot be given to that person in the future, then topical penicillin therapy may have to be discarded.

Brief mention is made of other substances used to enhance the therapeutic efficiency of penicillin in ointment mixtures.

# EFFECTS OF GLYCERITE OF HYDROGEN PEROXIDE ON INFECTIONS OF THE SKIN AND MUCOUS MEMBRANES

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ALTHOUGH previous studies have reported on the stability,<sup>1</sup> the antibacterial action,<sup>2</sup> the effects on tissue tolerance<sup>3</sup> and the clinical results achieved with glycerite of hydrogen peroxide in infectious conditions such as otitis media, these have been submitted or have appeared so recently that the composition and properties of the solution require brief description /

An analysis of the field of topical antiseptics demonstrates the fact that hydrogen peroxide possesses virtues which entitle it to a higher position than that which it holds in the opinions of students of this subject. It is true that in the presence of peroxidase its aqueous solutions decompose so rapidly that bacteria are little affected and that in the absence of peroxidase its effects are so mild that it has been given a low phenol coefficient. On the other hand, when its rate of decomposition can be controlled so that the effects of glycerite of hydrogen peroxide can be prolonged, the advantages of an inherently nontoxic, nonirritating and nonallergenic solution are immediately apparent.

Since pure hydrogen peroxide was not available when these studies were initiated, it occurred to Brown, Abramson and Gorin<sup>1</sup> that urea peroxide (a crystalline addition product) could be used to introduce hydrogen peroxide into a nonaqueous solvent both to enhance its stability in the absence of water and to prolong its effects by means of viscoidal solutions such as substantially anhydrous glycerin. It was subsequently discovered that some of the previous attempts in this direction had failed.

1 Brown, E A , Abramson, H A , Gorin, M , Kauffmann, H O , and Shanley, E C. The Stability of Urea Peroxide in Glycerol. *J Am Pharm A (Scient Ed)* **35** 304-306 (Oct) 1946

2 Brown, E A , Krabek, W , and Skiffington, R. A New Antiseptic Solution for Topical Application. Comparative in Vitro Studies, *New England J Med* **234** 468-472 (April 4) 1946

3 Brown, E A. Studies on Tissue Tolerance to a New Glycerol Peroxide Antiseptic Solution, *Ann Allergy* **4** 33-39 (Jan-Feb) 1946

because metallic trace elements in the glycerins used had inactivated the peroxides Oxine (8-hydroxyquimoline), which is itself bacteriostatic because it forms nonionizable salts of the metals necessary for normal bacterial metabolism,<sup>4</sup> acts similarly in solutions of glycerin, prolonging the stability of the peroxide

The solution now under investigation consists, therefore, of hydrogen peroxide (1.5 per cent) as derived from urea peroxide (4 per cent) dissolved in anhydrous glycerin to which has been added oxine (0.1 per cent) The peptizing and healing properties<sup>5</sup> and antibacterial action<sup>6</sup> of one of the end products, urea, are generally known, as is the bacteriostatic action of oxine<sup>4</sup> The glycerite of hydrogen peroxide solution demonstrates the antiseptic, deodorant, detergent and hemostatic properties of aqueous solutions of hydrogen peroxide except that these actions are prolonged The prolongation of such action is due solely to the surface tension of the glycerin, which confines the liberated oxygen to the solution As the liberated oxygen leaves the surface of the wound it continuously renews the interface at the infected surface, giving continued antiseptic effects The glycerin is churned into an oxygen-glycerin cream, which possesses the mechanical characteristics of both the liquid and the ointment type of topical application The effects of the glycerin, the urea and the oxine are entirely secondary to the action of the hydrogen peroxide

Tested by a modified agar cup plate method,<sup>2</sup> the solution has been shown to approach closely to tincture of iodine, U S P, in its bactericidal and bacteriostatic potency The studies on tissue tolerance<sup>7</sup> demonstrate a likelihood that at the 95 per cent level irritation might occur in less than 1 per cent of the general population

The first studies concerned with the treatment of infections dealt with acute and chronic conditions of the ear In one series<sup>8</sup> of 31 patients, 17 responded with complete remissions in fourteen days and in the remainder the condition cleared by the thirty-eighth day In the second series<sup>7</sup> the results were consistently duplicated

The present report describes the effects of the solution as used routinely in 120 patients presenting twenty-three clinical infectious enti-

4 Zentmayer, G A The Inhibition of Metal Catalysis as a Fungistatic Mechanism, *Science* **100** 294-295 (Sept 29) 1944

5 Robinson, W The Use of Urea to Stimulate Healing in Chronic Purulent Wounds, *Am J Surg* **33** 192-197 (Aug) 1936

6 Weinstein, L, and McDonald, A The Effect of Urea, Urethane and Other Carbamates on Bacterial Growth, *Science* **101** 44-45 (Jan 12) 1945

7 Brown, E A, and Kelemen, G The Use of Glycerite of Hydrogen Peroxide in Inflammatory Aural Conditions, *Laryngoscope* **56** 556-560 (Sept) 1946

8 Brown, E A, and Owen, W E The Treatment of Chronic Purulent Otitis Media with Glycerite of Hydrogen Peroxide, *Arch Otolaryng* **43** 605-612 (June) 1946

ties of the skin and mucous membranes. In some patients, two or more dermatologic conditions were present, as, for instance, aphthous stomatitis and paronychia.

In the group of patients studied, the sexes were almost equally represented. The greater majority were adult, the age range extending, however, from 7 to 81 years. In 54 patients, there were clinically recognizable mycotic infections, as dermatomycosis or onychomycosis. In 21 patients the infectious lesions were multiple, with affected toe nails in 11 and finger nails in 9. The clinical types were classified as vesicular (8 cases), squamous (7 cases) and pyodermic (6 cases). Additional sites of infection included the hands in 6 cases, the groin in 4, the perianal region in 3 and the axilla in 1. In 10 patients the ears were affected. Of these, 6 presented infections of the canal and 4 lesions of the junction of the pinna and scalp. In 2 patients there were classic examples of *erosio interdigitalis (monilia)* and in another 2 *tinea barbae*.

The organisms present were identified as *Trichophyton gypseum*, *Aspergillus glaucus*, monilia, mycelial filaments and yeastlike spores. Bacteria, especially staphylococci and streptococci, hemolytic and non-hemolytic, were consistently present as primary infection or as secondary invasion.

#### VESICULAR DERMATOPHYTOSIS

Eight patients presented pruritic, grouped and discrete vesicular lesions confined to the toes but occasionally involving the arch and lateral surface of the heel. A ten minute bath of the feet in aqueous solution of boric acid was prescribed, followed by an application twice daily for twenty minutes of the peroxide solution. All the patients responded with complete remission.

#### SQUAMOUS DERMATOPHYTOSIS

Seven patients presented scaling, fissuring, pruritic lesions of the toes and the toe webs. Infections of the third or fourth interspaces associated with thickened, sodden, adherent epidermis required two to three weeks of two applications daily, the other scaling lesions clearing in three to five days.

#### PUSTULAR DERMATOPHYTOSIS

The 6 patients with pustular dermatophytosis presented acute vesiculobullous and pustular lesions characterized by sudden onset, intense pruritus, pain and edema, followed by fissuring, exfoliation and serous oozing and crusting. The bordering red, punctate, papular, discrete and confluent lesions were present. In all patients there was a subsequent exfoliation and dyshidrosis. All required rest in bed. During the acute stage of the eruption continuous wet dressings with boric

acid, isotonic solution of sodium chloride or solution of aluminum acetate (1:30) were used. Glycerite of hydrogen peroxide was applied topically for ten to twenty minutes four times daily and removed with surface sponging with warm water or aqueous solution of zephiran chloride (1:1,000). The bullae and vesicles were punctured, exfoliated epidermis was removed and the nails clipped short.

After the acute process had subsided, glycerite of hydrogen peroxide alone was applied twice daily for five to ten minutes and sponged off with warm water. Subsequent treatment included low voltage roentgen rays (80 r unfiltered) at intervals of seven to fourteen days.

Each of the 6 patients in the group returned to his work within two weeks. In 1 patient undergoing his third attack of acute dermatophytosis with a generalized secondary sensitization dermatitis, the glycerite of hydrogen peroxide produced an effect resembling mild dermatitis venenata, and its use was, therefore, discontinued.

#### TINEA CRURIS

In 8 patients presenting chronic mycotic infections of the groin, perianal and axillary areas, the results were indifferent. In 3 patients, the topical applications were found to be stimulating to the point of irritation. In the others, applications twice daily afforded relief, but not one patient responded with complete recovery.

#### PARONYCHIA

In 3 patients with paronychia, recovery occurred in three days for 1 and in two weeks for the remaining 2, the solution having been applied as a wet dressing for twenty minutes five times daily.

#### ONYCHOMYCOSIS

In 5 of the 20 patients presenting onychomycosis, radical removal of the nails was necessary. In 15 the nails were clipped as short as possible. In the first 5 patients, the nail bed was bathed with glycerite of hydrogen peroxide 1:15 for ten minutes twice daily and boric acid ointment dressing applied between applications. In all 5 cases, new nails, free of infection, grew normally. The 15 remaining patients soaked their affected nails in aqueous solution of boric acid for thirty minutes daily and applied the glycerite of hydrogen peroxide for ten minutes or longer each day. Although all demonstrated objective improvement, in none was the mycotic involvement completely eradicated. It would appear that in this type of lesion more intimate contact and more prolonged application are necessary to affect the responsible organisms.

#### TINEA OF THE HANDS

All 3 patients with tinea of the hands presented the typical intracutaneous vesicular and pustular lesions. The intracutaneous vesicles

were denuded and after soaks in aqueous solution of boric acid, glycerite of hydrogen peroxide was applied topically. In 2 patients there was complete recovery but in the third, who presented a secondary type of id eruption, the solution appeared to cause irritation, and its use had to be discontinued.

#### EROSIO INTERDIGITALIS (MONILIAL)

Two patients presented three typical lesions characteristically involving the web of the third and fourth fingers. The lesions were sharply defined, superficially inflamed, chronic and recalcitrant. Yeastlike organisms were demonstrated in scrapings from the borders of the lesions. The treatment consisted in keeping the hands as free as possible from contact irritants, the surface of the lesions being denuded by gentle scrubbing with a soft brush and aqueous solution of boric acid. Moist dressings of glycerite of hydrogen peroxide were applied continuously. All three lesions cleared completely after two to three weeks of treatment.

#### TINEA OF THE EXTERNAL EAR

In 10 patients of this series there were chronic or recurrent infections of the external ear, of the external auditory canal in 6 and of the junction of the scalp and ear in 4. The lesions were chronic, edematous, inflammatory and painful, with fissuring, exfoliation and cellulitis. The lesions were sponged twice daily with aqueous solution of boric acid or with aqueous solution of zephiran chloride (1:1,000) and dried. The glycerite of hydrogen peroxide was applied for thirty minutes daily. In each case the pruritus was completely controlled, the pain relieved and recovery complete in seven to twenty-eight days.

#### TINEA BARBAE

In each of the 2 patients with tinea barbae the topical applications of glycerite of hydrogen peroxide proved irritating, and within four days its use had to be discontinued.

#### LESIONS OF THE MOUTH

The 20 patients with lesions of the mouth presented one or more of the following diseases: aphthae, herpes simplex, gingivitis, lingual tonsillitis, epidermolysis bullosa with oral lesions, traumatic lesions due to a dental plate or to dental extractions, postoperative infections or fissuring of the lips.

In these patients, the glycerite of hydrogen peroxide (1.5 per cent) was diluted 1:15 and prepared immediately before being used routinely as a mouth wash and gargle four times daily, after meals and at bedtime. The clinical effects are listed later.

## APHTHOUS STOMATITIS

Of 2 patients, stomatitis had been present in 1 for twelve years and in the other for three years. The lesions were multiple, painful, shallow, inflammatory ulcers varying from 4 mm to 1.2 cm in diameter. Both patients were vaccinated with smallpox vaccine, the first twice without success. In the second an intense local reaction and a successful "take" developed.

The diluted glycerite of hydrogen peroxide was used three times daily and at bedtime, the lesions clearing completely, although no previous remission had lasted for more than a few days. The results in the treatment of this disease were so striking as to raise the question as to whether or not the virus causing the lesions might be constantly present in the mouth, its destruction by oxidation removing the local cause. This problem requires further investigation.

## HERPES SIMPLEX

Five patients presenting typical localized grouped vesicular lesions on, near or immediately within the margin of the lip responded with complete healing in four to six days following topical application of glycerite of hydrogen peroxide several times daily.

## GINGIVITIS

The 4 patients with chronic bleeding, spongy gums, in all of whom Vincent's organisms could be demonstrated, responded readily to applications of glycerite of hydrogen peroxide used twice daily as a mouth wash. A separate report regarding the use of the solution in infections of the mouth is now in preparation.

## LINGUAL TONSILLITIS

Two patients presenting painful lingual tonsillitis with injection of the tonsillar pillars and inflammation of the posterior pharyngeal wall used glycerite of hydrogen peroxide, dilute solution, as a gargle five times daily, with complete relief within one day.

## TRAUMATIC ORAL LESIONS

In 2 patients who had had badly fitted lower dental plates there were irregular, deep, linear infected and painful ulcerations in the left side of the floor of the mouth. A thin, milky, leukoplakia-like discoloration involved the immediately surrounding mucosa. The ulcers had been persistently present for several weeks despite the fact that the plates had not been used during that time. The dilute solution of glycerite of hydrogen peroxide used as a mouth wash after meals brought complete recovery within twelve days.

In 1 patient who had twelve teeth extracted ten days before presenting himself for treatment, the gums were still loose and spongy and not

healing There was an obvious fetor The dilute solution of glycerite of hydrogen peroxide used as a mouth wash thrice daily produced a firm healing of the gums, so that within two weeks the patient could be properly fitted for a dental plate

In 2 patients presenting postoperative infected lesions, the first a leukoplakia and the second a mucous retention cyst of the lower lip, the dilute solution was given as a mouth wash, both patients responding with complete remission

#### FISSURE OF THE LIP

In a single instance a chronic, deep vertical, painful fissure running from the midportion of the mucosa of the lower lip healed in ten days following topical application of the undiluted solution of glycerite of hydrogen peroxide applied five times daily

#### EPIDERMOLYSIS BULLOSA

The 1 patient with epidermolysis bullosa, a woman aged 28, had suffered since August 1943 with a continuous, painful, oral, vesicular and bullous ulcerative eruption of the tongue, lips, buccal mucosa, throat and palate, all or any of which were involved at one time or another The patient was presented at the Boston meeting of the Atlantic Dermatological Society (Feb 9, 1946) The dilute solution of glycerite of hydrogen peroxide has proved itself to be the most efficacious preparation she has so far used, partially controlling the ulceration and completely relieving the pain The disappearance of the lesions has not been complete, but the relief attained merits continued irrigations

#### IMPETIGO CONTAGIOSA

In 3 patients with impetigo, an aqueous solution of boric acid was used to keep the crusts removed from the facial lesions and the glycerite of hydrogen peroxide solution applied several times daily Complete recovery occurred in three to five days

#### WOUNDS, LACERATIONS AND LOCAL INFECTIONS

In more than 50 patients in whom glycerite of hydrogen peroxide was used postoperatively to sterilize the operative site after completion of a surgical procedure, not one failed to heal by first intention No infection of any type was noted

When the solution was used to prevent infection, a single application for two or three minutes was sufficient When used to irrigate and sterilize local abscesses and the incised lesions of furunculosis, a ten minute application or irrigation twice daily prevented infection After each application, the material was sponged from the surface of the surrounding skin and a proprietary boric acid ointment or a dry dressing applied

Two patients with axillary furunculosis, another with furunculosis of the groin, 2 with furunculosis of the neck and 1 each with furuncles of the ear and leg made rapid and favorable response to this procedure.

Two patients presenting large infected cysts, which were painfully inflamed and swollen, had irrigations with glycerite of hydrogen peroxide following incision and drainage. In both the lesions healed completely within eight days. Three patients in this group merit detailed description. The first, a man aged 53, presented an infected sinus in the scar of a postoperative fractured patella. The scar consisted of six sinus openings, each bathed in pus and filled with granulation tissue. Cultures proved beta hemolytic streptococci, *Staphylococcus albus*, a few gram-positive cocci and a rare gram-positive bacillus to be present. The sinuses were irrigated twice daily with the solution of glycerite of hydrogen peroxide. Exploration proved the presence of six long, black, silk sutures, which were removed. The infection cleared with the continued irrigation, and the lesion healed within two months.

In the second patient, a man aged 84, contact dermatitis developed on the dorsa of the hands while he was handling brass pipe and a synthetic wool used for packing. A secondary infection occurred associated with lymphangitis and tender epitrochlear and axillary glands, present bilaterally. Deep multilocular abscesses developed in the tissue of the left biceps muscle. Laboratory studies proved *Staph aureus* and gram-positive cocci to be present. The patient was hospitalized and the abscesses irrigated with glycerite of hydrogen peroxide, the solution being applied undiluted as a moist dressing between irrigations, which were done twice daily. During the day dressings of isotonic solution of sodium chloride were applied and during the night a proprietary boric acid ointment. Complete recovery occurred in ten days.

The third patient, aged 68, presented at the New England Dermatological Society (February 1945), had suffered for thirty-eight years from chronic liquefying nodular panniculitis of an afebrile type involving the legs. Painful ulcerations occurred in crops, the onset of each lesion being marked by a pink macule 2 to 4 mm in diameter superimposed on a tender nodule 2 mm in diameter. These lesions gradually enlarged to form a painful bluishly discolored nodule 2 to 4 cm in diameter, which eventually broke down with a serosanguinous discharge. Subsequent healing was extremely slow and left a depressed atrophic scar.

Cultures, smears, biopsies and inoculations of a guinea pig failed to reveal any organism, although stained smears demonstrated 14 to 200 leukocytes present in each oil immersion field. The solution of glycerite of hydrogen peroxide used undiluted as an irrigation brought immediate relief from pain and prompt healing of the lesions within ten days, although all previous exacerbations had required three to four weeks for recovery.

#### PUSTULAR PSORIASIS

In 3 patients with pustular psoriasis affecting the palms, soles, heels, finger nails or scalp, there was no effect following the application of glycerite of hydrogen peroxide

#### SOLAR DERMATITIS

In 2 patients who invariably presented pinhead-sized acuminate papules over the cheeks, nose, chin and ears following exposure to the sun, the topical application of glycerite of hydrogen peroxide was ineffective

#### SENSITIZATION DERMATITIS

In 4 patients presenting typical sensitization dermatitis on the feet and on the hands, the solution was not effective and actually proved too irritating for continued use

#### VERRUCAE

In 10 patients presenting verrucae of the plantar, palmar, periungual and subungual areas, the solution was either applied as a moist dressing constantly for two weeks or at intervals of thirty minutes twice daily or applied to the sheared verrucae at a point at which punctate bleeding occurred. In no instance was the solution effective. In view of the fact that the solution liberates oxygen, it was not injected into the base of any wart

#### SUMMARY

The composition and properties of a new antiseptic solution, glycerite of hydrogen peroxide, are described

Its effects on the cutaneous manifestations of 120 patients, comprising twenty-three clinical entities of the skin and mucous membranes studied over a period of fifteen months, are listed. Since there is at the present no adequate method for making control studies in clinical investigations of this type, we are purposefully limiting our comments to the descriptions of the exact results as recorded in the body of this paper

The use of the solution in 50 additional patients as a postoperative dressing was marked by an absence of secondary infection

Although not effective in the treatment of psoriasis, solar dermatitis and verrucae and apparently causing irritation in some cases of tinea barbae and tinea cruris as well as in sensitization dermatitis, it appears effectively to lessen infection and hasten healing time in primary fungous and primary and secondary bacterial infections

The clinical courses of certain types of virus infections seem favorably influenced by its use

# EOSINOPHILIC GRANULOMA OF BONE WITH CUTANEOUS MANIFESTATIONS

Report of a Case

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AND

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INTEREST of pathologists and orthopedic surgeons has within recent years been focused on a newly classified group of diseases, comprising Hand-Schuller-Christian disease, a relative newcomer, assigned the eponym Letterer-Siwe disease, and a third, variously known as eosinophilic or destructive granuloma of bone. Occurrence of both cutaneous lesions and visceral involvement as prominent accompaniments of these processes recommends further study and investigation by dermatologist and internist.

Letterer-Siwe disease, so titled because of the original description by Letterer and the subsequent collection and grouping of cases by Siwe<sup>1</sup> appears to be the severest, eosinophilic granuloma the mildest and Hand-Schuller-Christian disease the intermediate manifestation of an identical underlying basic disease.<sup>2</sup> This classification necessitates withdrawal of Hand-Schuller-Christian disease from its previously held position in the group known as diseases of lipid metabolism, remaining members of which are Gaucher's disease and Niemann-Pick disease. Recent investigations lend weight to the accuracy of this reshuffling. While the case to be reported is regarded primarily as one of eosinophilic granuloma

Dr Cawley is from the service of Dr U J Wile and Dr A C Curtis

Studies and contributions from the Department of Dermatology and Syphilology, University of Michigan Medical School

1 Abt, A F, and Denenholz, E J Letterer-Siwe's Disease Spleno-hepatomegaly Associated with Widespread Hyperplasia of Nonlipoid-Storing Macrophages, Discussion of the So-Called Reticuloendothelioses, *Am J Dis Child* **51** 499 (March) 1936

2 (a) Green, W T, Farber, S, and McDermott, L J Eosinophilic or Solitary Granuloma of Bone, *J Bone & Joint Surg* **24** 499 (July) 1942 (b) Gross, P, and Jacob, H W Eosinophilic Granuloma and Certain Other Reticulo-Endothelial Hyperplasias of Bone A Comparison of Clinical, Radiologic and Pathologic Features, *Am J M Sc* **203** 673 (May) 1942 (c) Jaffe, H L, and Lichtenstein, L Eosinophilic Granuloma of Bone A Condition Affecting One, Several, or Many Bones, but Apparently Limited to the Skeleton, and Representing the Mildest Clinical Expression of the Peculiar Inflammatory Histiocytosis, also Underlying Letterer-Siwe Disease and Schuller-Christian Disease, *Arch Path* **37** 99 (Feb) 1944

of bone with cutaneous manifestations, the interrelationship of the three processes is apparently close, entailing a brief description of Letterer-Siwe disease and Hand-Schuller-Christian disease as well as eosinophilic granuloma.

Occurrence in extremely young persons, usually before the age of 2 or 3, severity of the process and extensive generalized involvement can be predicated for Letterer-Siwe disease. Analysis of 9 cases<sup>1</sup> and reports of others paint a fairly typical picture of this disease. Destructive osseous lesions are frequent, and these apparently have a special predilection for the calvarium.<sup>2c</sup> Most frequently confused with these punched-out defects on roentgenographic study are cysts of the bone, metastatic neoplasm and multiple myeloma. Persistent low grade fever is common, and secondary anemia is present relatively often. Hepatomegaly and splenomegaly, with, in addition, enlargement of lymph nodes, occur almost without exception. Cutaneous manifestations have been described as superficial ulcerations of the skin, petechiae, purpura, ecchymoses and combinations of the last three, the hemorrhagic tendency being apparently most pronounced shortly before death. The course pursued is oftenest acute or semichronic, generally fatal in a matter of weeks to two years, although in some cases the condition apparently becomes definitely chronic and passes into the realm of Hand-Schuller-Christian disease.<sup>2c</sup>

Most thoroughly studied and probably best known of the three conditions, Hand-Schuller-Christian disease may at times bear a decided resemblance, clinically and even from a histologic standpoint, to Letterer-Siwe disease and eosinophilic granuloma of bone. Destructive skeletal lesions are relatively common in conjunction with Hand-Schuller-Christian disease, although in an analysis of 84 previously reported cases, 2 with involvement of the soft tissues, but none with roentgenologic evidence of bony lesions were uncovered.<sup>2b</sup> Complete or partial absence of the textbook triad, which embraces diabetes insipidus and exophthalmos in addition to bony defects of the cranium, has been emphasized by several investigators. Presence of one or more is suggestive, and the occurrence of hepatomegaly and splenomegaly, in addition, places emphasis on this disease as a diagnostic possibility. Retarded physical development is not uncommon. Cutaneous lesions, occurring in approximately one third of the cases, have received special attention on at least one recent occasion. A diffuse petechial efflorescence in association with acute manifestations of the disease, and papules or nodules accompanying chronic forms are apparently encountered most frequently.<sup>3</sup>

3 Lane, C. W., and Smith, M. G. Cutaneous Manifestations of Chronic (Idiopathic) Lipoidosis (Hand-Schuller-Christian Disease), *Arch. Dermat. & Syph.* 39: 617 (April) 1939.

Various observers have given the mortality rate as approximating 30 per cent

Description, discussion and study of eosinophilic granuloma, the third and least severe of this group, have been rather extensive in the past few years. In the preponderance of reported cases the condition has occurred in children and young adults. Complete absence of or a minimum of general manifestations is the rule, although localized symptoms referable to the bony lesions, such as pain and swelling, occur with a fair degree of frequency. The destructive osseous lesions, which may suggest Hand-Schuller-Christian disease, Letterer-Siwe disease, cysts of the bone,



Fig 1—Discrete, granulomatous papules with a moist surface as they appeared in the right axilla in the reported case

malignant growth or multiple myeloma to a roentgenologist, are solitary or multiple, a maximum of twenty-five in 1 case having been reported. Flat bones are involved oftenest.<sup>4</sup> Laboratory studies usually present no significant alteration from the normal, although moderate leukocytosis and at times a peripheral eosinophilia of mild degree may be encountered. Cutaneous manifestations, with the exception of one casual reference,<sup>4</sup> have apparently not previously been reported. Prognosis based on cases hitherto described, appears to be uniformly good, although occur-

4 Farber, S. The Nature of "Solitary or Eosinophilic Granuloma" of Bone, *Am J Path* **17** 625 (July) 1941

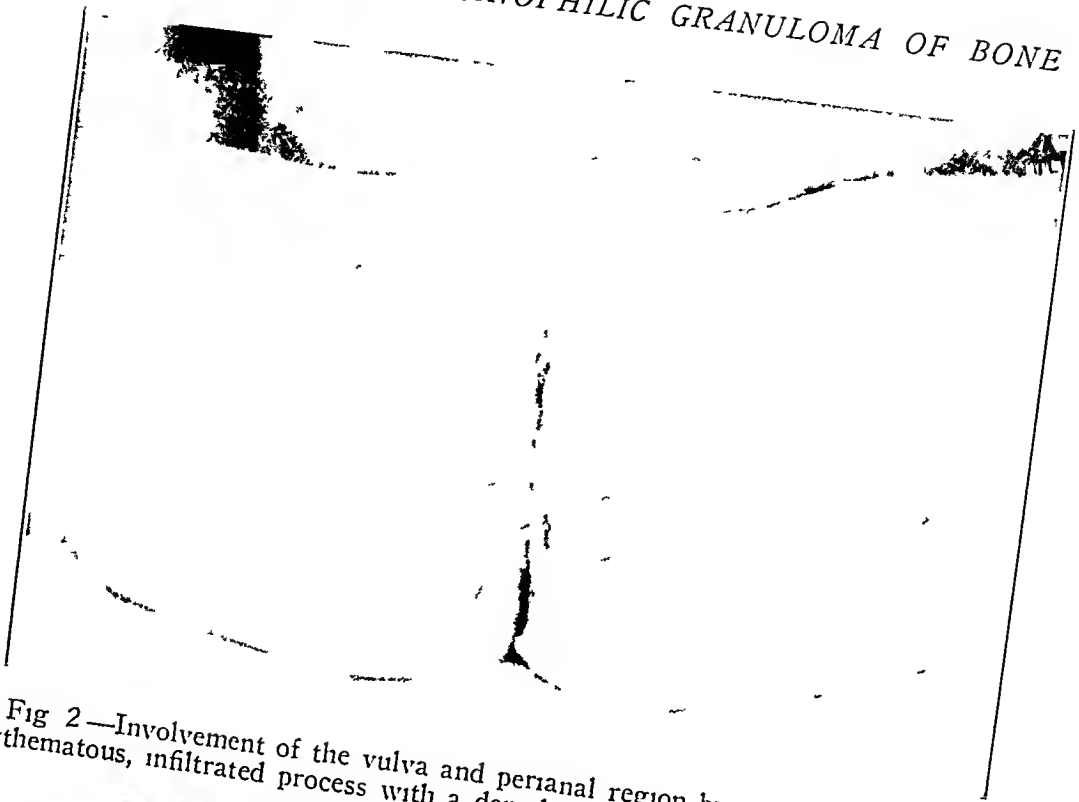


Fig 2—Involvement of the vulva and perianal region by a sharply demarcated, erythematous, infiltrated process with a denuded weeping surface



Fig 3—Destructive osseous lesion involving the left ilium. Further roentgenologic examination, subsequent to the administration of roentgen ray therapy, demonstrated complete healing of this as well as other bony lesions

rence of destructive bony lesions at vital sites<sup>5</sup> may occasion considerable apprehension until the process is controlled. Roentgen therapy, curettage of the osseous lesions or a combination of the two is usually productive of a satisfactory result, and spontaneous healing has been recorded.

As previously described, Letterer-Siwe disease, Hand-Schuller-Christian disease and eosinophilic granuloma are believed by most investigators to be individual manifestations of an identical basic process, the exact nature of which has not been determined. One competent observer has expressed the opinion that "a satisfactory working classi-



Fig 4—Involvement of the axillary portion of the right second rib with a process similar to that in the ilium

fication of these conditions should include the three separate clinical types of Hand-Schuller-Christian disease, Letterer-Siwe disease and eosinophilic granuloma of bone, with transitional forms between eosinophilic granuloma and each of the other two diseases in this group"<sup>6</sup>. The etiologic factor cannot yet be stated, although trauma and possibly infection may play a part. Histopathologic studies of the lesions have probably been most suggestive of the interrelationship of these three condi-

5 Osborne, R. L., Freis, E. D., and Levin, A. G. Eosinophilic Granuloma of Bone Presenting Neurologic Signs and Symptoms. Report of a Case, *Arch Neurol & Psychiat* **51** 452 (May) 1944.

6 Farber, S. The Nature of Some Diseases Ascribed to Disorders of Lipid Metabolism, *Am J Dis Child* **68** 350 (Nov) 1944.

tions, the findings having been described in detail and in excellent fashion by several of the authors previously cited. Salient points are these: abundance of histiocytes with varying numbers of eosinophils characterize most cases of eosinophilic granuloma, the presence of eosinophils being also at times a feature of Hand-Schüller-Christian disease. Osseous lesions of Letterer-Siwe disease, more particularly early ones, apparently demonstrate infiltration by eosinophils, while lesions of the soft tissue



Fig 5—Roentgenologic examination of the skull demonstrated this bony lesion in the vicinity of the antrum, right mastoid

are said not to present this cytologic picture.<sup>2c</sup> Changes in the bone marrow of various description occur in most cases of Letterer-Siwe disease<sup>1</sup> and are a not uncommon accompaniment of eosinophilic granuloma.

#### REPORT OF A CASE

In September 1944, G. C., a 16 month old girl from Detroit, was referred to the Dermatology Clinic of the University of Michigan Hospital because of a cutaneous eruption. The child had been as well as usual until the age of 8 months, at which time an eruption similar to seborrheic dermatitis appeared on the scalp.

About the same time, small, red, discrete and coalescent papules became apparent on the buttocks and about the genitalia and erythematous, painful, eroded patches appeared in various parts of the mouth. Shortly thereafter, lesions similar to those on the buttocks and about the genitalia were noted on the soles and between the toes. Despite local therapy the entire process became steadily worse, and the child was seen in the clinic for the first time on Sept 14, 1944.

The consulting dermatologist described his findings thus: "Over the palate and on the posterior aspect of the tongue are small, grayish white, circumscribed macules. Sharply demarcated, erythematous papules, 2 to 3 cm in diameter, with a weeping, granulomatous surface are present in each axilla. Over the abdomen and in both inguinal regions are erythematous, scaling papules 1 to 2 mm in

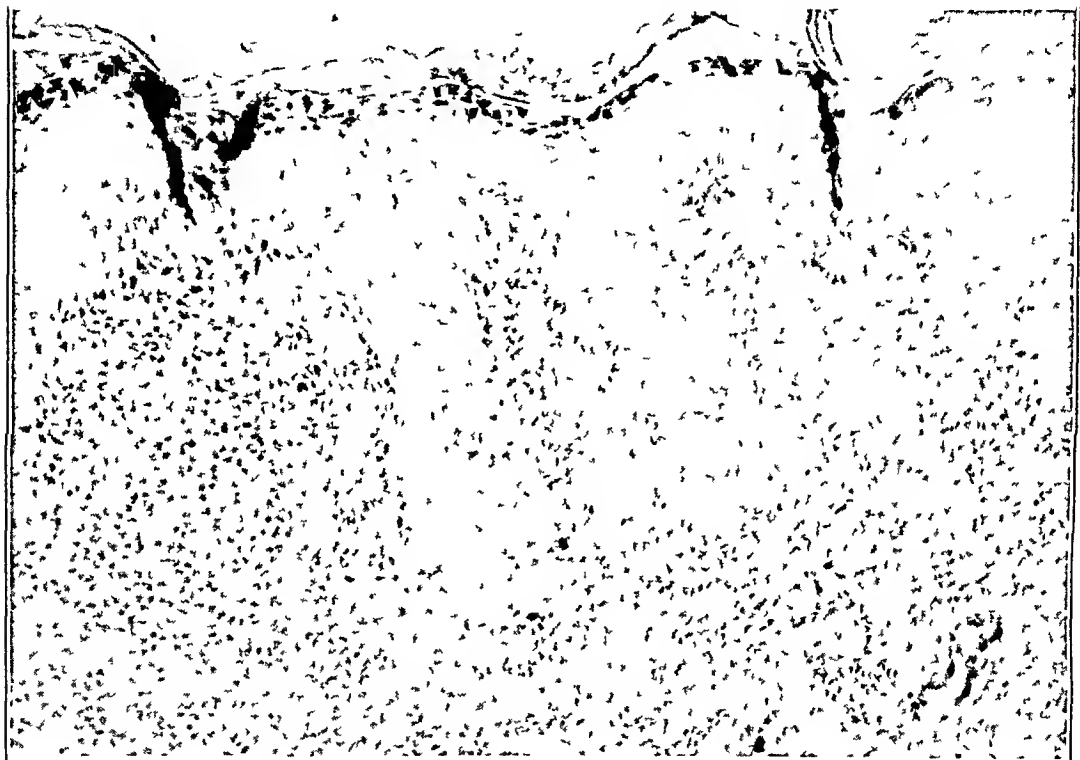


Fig 6—Photomicrograph made from a section of one of the cutaneous lesions, showing an infiltrate limited chiefly to the dermis (low power)

diameter, while the genitalia and perianal region are involved by an edematous process with a denuded, weeping surface.

Biopsy specimens were taken from lesions in the right axilla and those on the buttocks and abdomen. Microscopically, all showed the same essential lesion, which at first glance resembled a malignant process, being especially suggestive of reticuloendothelioblastoma. Detailed examination, however, revealed all cells of the infiltrate to be well differentiated, with an abundance of histiocytes and in places a great many eosinophils, a picture compatible with, in the opinion of two authorities,<sup>7</sup> eosinophilic granuloma of bone or Letterer-Siwe disease manifesting cutaneous lesions.

<sup>7</sup> Montgomery, H. Personal communication to the authors. Farber, S. Personal communication to the authors.

Roentgenologic examination of the skull, chest, long bones and spine demonstrated a destructive lesion involving the axillary portion of the second rib on the right side with an overlying swelling of the soft tissue, in addition to a similar destructive lesion in the left ilium. A similar lesion subsequently developed in the right mastoid. Biopsies of these were not obtained.

During her stay in the hospital the child was not febrile. The liver and spleen were not and did not become palpable, but there were a few small, nontender lymph nodes in both cervical and inguinal regions. A complete blood cell count on several occasions showed no significant alteration from the normal other than a slight toxic granulation of the neutrophils and a sedimentation rate of 27 mm per hour. No eosinophils were counted. Tibial aspiration was also made. The hematologist reported, "Neither the blood nor the marrow presents definite evidence of neoplastic involvement." The Kahn reaction of the blood was negative, and the urine was normal.

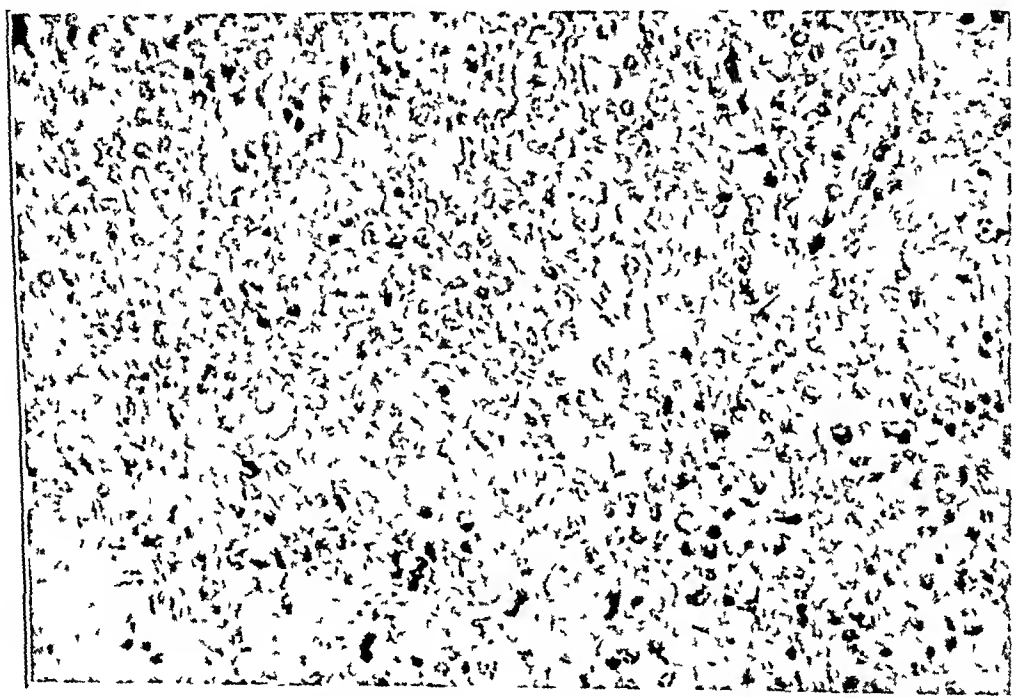


Fig 7—High power photomicrograph of the infiltrate shown in figure 6, demonstrating a reticulum containing many histiocytes with varying numbers of interspersed eosinophils.

Following roentgen therapy<sup>8</sup> to the lesions of the bone, as well as to the cutaneous eruption, there was complete but gradual healing, over a period of months, of the former, while the cutaneous manifestations had cleared almost completely at the time the child was last seen. Further skeletal or cutaneous lesions did not occur.

NOTE—This case was presented and discussed as an example of eosinophilic granuloma of bone with cutaneous manifestations at the annual meeting of the Central States Dermatological Society in Detroit, on April 27, 1946.

8 Five hundred roentgens were delivered to the osseous lesions through 0.5 mm of copper and 1.9 mm of aluminum, 300 to 600 r, unfiltered and in divided doses, were delivered to the cutaneous eruption, 1,500 r were delivered to the oral cavity through 0.5 mm of copper and 1.0 mm of aluminum, given in divided doses over a period of several months.

## SUMMARY

Letterer-Siwe disease, Hand-Schüller-Christian disease and eosinophilic granuloma of bone appear to merit classification as closely allied manifestations, varying chiefly in severity, of a basic disease, the exact nature of which is not known. Cutaneous lesions are of frequent occurrence with the first two but have not been described, so far as known, in conjunction with the last. A case presenting findings compatible with a diagnosis of eosinophilic granuloma of bone and demonstrating cutaneous lesions as a part of the process is reported. Roentgen and radiation of both osseous and cutaneous lesions gave satisfactory therapeutic results.

# PACHYONYCHIA CONGENITA

Report of Two Cases, with Studies on Therapy

CARROLL S WRIGHT, M D

AND

JACQUES P GUEQUIERRE, M D

PHILADELPHIA

**P**ACHYONYCHIA congenita is a rare congenital anomaly, originally described under this name by Jadassohn and Lewandowsky<sup>1</sup> The literature was thoroughly reviewed in 1934 by Diasio,<sup>2</sup> who reported that Heller had previously called attention to the close resemblance between the condition reported by Jadassohn and Lewandowsky and the syndrome described under the caption "congenital dyskeratosis" by Erich Schafer Schafer's observations were based on 1 case of his own and 13 culled from the literature In 1935 Sohrweide<sup>3</sup> reported a case under the name "pachyonychia ichthyosiformis"

Ormsby<sup>4</sup> in 1943 recognized the title "pachyonychia congenita" and summarized the characteristics as follows

dystrophic changes in the nails, palmar and plantar hyperkeratosis, anomalies of the hair, leukoplakia, follicular keratoses of the acne-form type particularly about the knees and elbows and dyskeratosis of the cornea Verrucous lesions are described as occurring on the knees, elbows, popliteal regions, buttocks, legs and ankles Bullae are common and occur chiefly on the plantar surfaces of the feet Generalized ichthyosis of variable degree may or may not be present The affection occurs chiefly with the male sex In all of the reported cases pachyonychia has been present All of the associated symptoms above mentioned have occurred in whole or in part in the various cases recorded

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Read at the Sixty-Sixth Annual Meeting of the American Dermatological Association, Hot Springs, Va, June 10, 1946

1 Jadassohn, J, and Lewandowsky, in Neisser, A, and Jacobi, E *Ikonographia dermatologica*, Berlin, Urban & Schwarzenberg, 1907, cited by Diasio<sup>2</sup>

2 Diasio, F A Pachyonychia Congenita Jadassohn A Variety of Ichthyosis (Pachyonychia Ichthyosiformis) Involving Chiefly the Nails, *Arch Dermat & Syph* **30** 218-226 (Aug) 1934

3 Sohrweide, A W Pachyonychia Congenita Report of a Case, *Arch Dermat & Syph* **32** 370-376 (Sept) 1935

4 Ormsby, O S, and Montgomery, H *Diseases of the Skin*, ed 6, Philadelphia Lea & Febiger, 1943

An excellent description of the microscopic picture of the skin is given by Andrews<sup>5</sup>

The striking feature of the specimen was a thickening of the epidermis due to acanthosis and parakeratosis, especially pronounced about the pilosebaceous follicles. The rete pegs were lengthened, and about the follicles the epidermal thickening caused funnel-shaped prolongations extending into the corium. The openings of the follicles were dilated and plugged with imperfectly cornified and somewhat degenerated horny material, and horny plugs were also present in the sweat pores. The basal cell layer was irregular and the cells were swollen. There was granular degeneration in the prickle cells, the nuclei stained deeply, and some were crescentic, being pushed to one side of the cell by hydrops. They resembled the *corps ronds* found in cases of Darier's disease. The papillary bodies between the rete pegs were elongated, and in some places the apices came near the



Fig 1—Pachyonychia congenita, showing the thickening of the finger nails and the keratotic lesions of the skin

surface of the skin. The blood vessels of the corium were dilated and surrounded by lymphocytes, mast cells, connective tissue cells and an occasional plasma cell, the appearance suggested a mild inflammation from the pressure or irritation of the overlying thickened epidermis. The connective tissue seemed normal.

#### REPORT OF TWO CASES

CASE 1—I L, a white boy, was first admitted to the Temple University Hospital in 1936, at the age of 6. At birth the entire cutaneous envelope was rough and the thumb nails appeared to be "infected." When he was 2 years old "blisters" had formed on the soles, knees and elbows. These ruptured, with the formation of loosely bound crusts. The nails of the hands and feet developed

<sup>5</sup> Andrews, G. C. Pachyonychia Congenita, Arch Dermat & Syph **33** 183-184 (Jan) 1936

abnormally, becoming extremely thick. When the patient was examined at the Temple University Hospital in 1936, a diagnosis of "ectodermal defect" was made and a section of skin submitted to the laboratory. The report on this section was as follows: "Microscopic study revealed small sections of skin showing decided irregularity of the surface with extensive hyperkeratosis. There were small narginations of the surface epithelium filled in by horny plugs. The epithelial cells showed dyskeratosis and small areas of parakeratosis. The picture suggested sorospermosis follicularis vegetans of Darier."

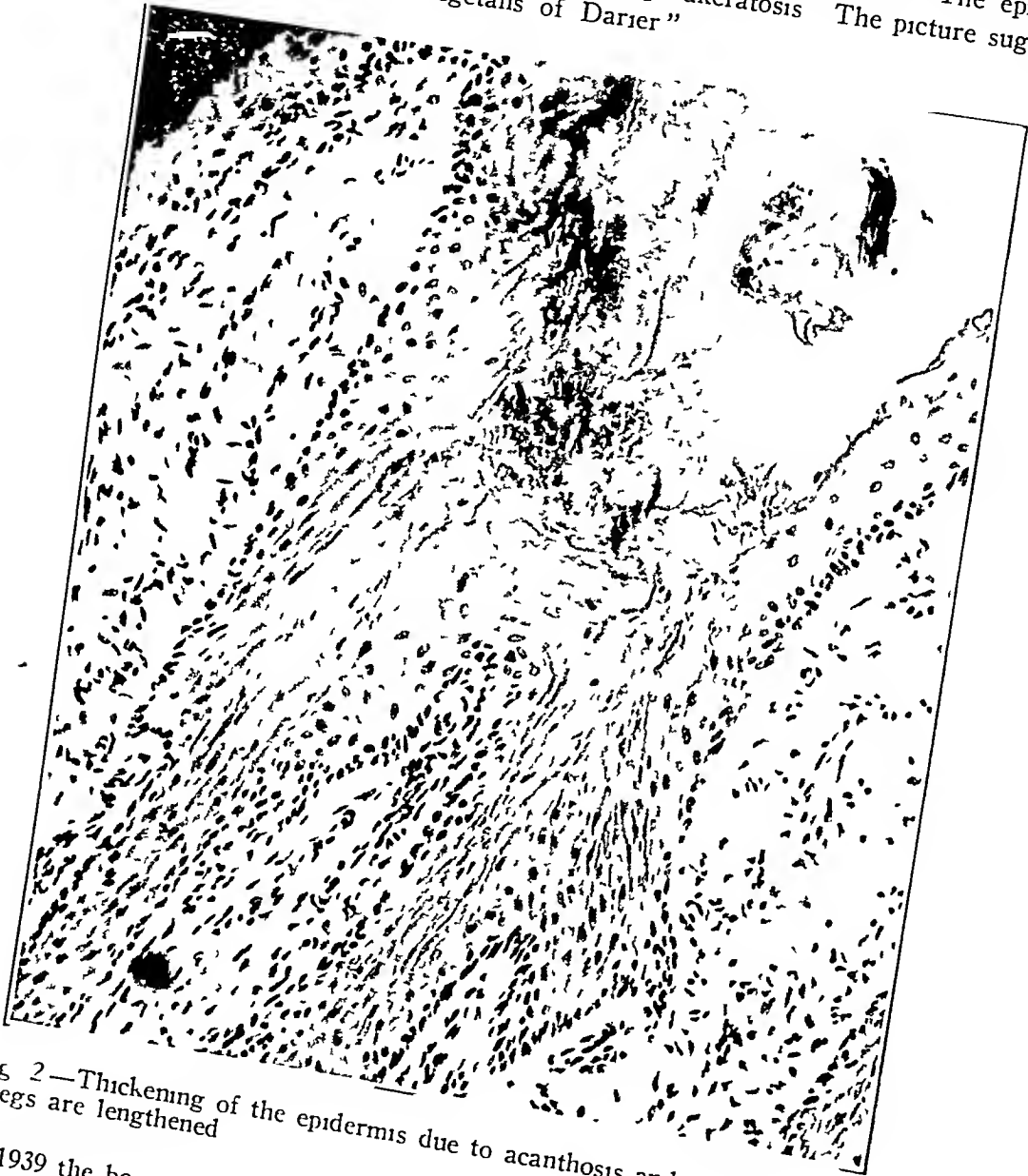


FIG. 2—Thickening of the epidermis due to acanthosis and parakeratosis. The rete pegs are lengthened.

In 1939 the boy was admitted to the Harriet Lane Home for Invalid Children at Johns Hopkins Hospital, with a diagnosis of "chronic eczema secondarily infected producing an impetiginous picture." The infected lesions were treated with compresses of chlorazodin, potassium permanganate and gentian violet medicinal, after which they healed for a period of six months. New erosive and infected lesions then appeared, and they persisted until the patient was readmitted to Johns Hopkins Hospital in April 1940. In addition to the open lesions the skin at that time was generally rough, and the tongue, gingiva and buccal mucosa

revealed "a diffuse, superficial, leukoplakic involvement" The diagnosis made was "congenital ectodermal dysplasia of as yet unclassified type with secondary infection" At that time the laboratory findings were as follows hemoglobin content 100 per cent, white blood cells 10,000, differential count normal, urine normal, serum protein content 5.9 Gm per hundred cubic centimeters, albumin-globulin ratio 1.3, serum cholesterol level 161 mg, results of roentgenologic examination of the gastrointestinal tract normal, scrapings of the skin negative for fungi, blood Wassermann reaction negative, and tuberculin reaction (to 0.1 mg) negative

In June 1942 the boy was readmitted to the Temple University Hospital for further study, and between that date and June 1945 there was a total of six admissions, varying in length from a few days to several weeks Observations at examination in 1942 were as follows "The skin was generally dry and thick-



Fig 3—Pachyonychia congenita, illustrating crusted cutaneous lesions and thickening of the toe nails

ened, with many elevated lesions resembling keratotic plugs, particularly over the shoulders, elbows and knees The feet had denuded, crusted patches extending from the soles up the medial and lateral aspects Removal of the crusts revealed reddened bases having a shiny or somewhat glazed appearance The hair was dry and lusterless The buccal mucosa and tongue showed patches suggestive of leukoplakia Most striking were the changes in the nails The nails of the hands and feet were greatly thickened, some to a depth of  $\frac{1}{2}$  inch (1.2 cm) The growth of the nail appeared to be away from the nail matrix rather than from the nail root"

The boy and his parents were chiefly interested in therapy for the crusted inflammatory patches and the nails Because of the overgrowth of the nail plate he was able to make but little use of his fingers Wet dressings of buffered

cysteine hydrochloride, as described by Goldberg,<sup>6</sup> were continuously applied to the crusted areas, and within ten days all lesions were healed (It is worthy to note that during subsequent recurrent outbreaks of these inflammatory crusted lesions various other applications were tried, but invariably it was necessary to use the buffered cysteine hydrochloride to bring about healing )

A consultation with a member of the surgical staff, Dr George Rosemond, was requested, and the decision was reached to remove the nail plates completely with the patient under general anesthesia This was done Nov 17, 1942 and the patient sent home In June 1943 the patient returned, showing only a partial return of the thickening of the nail plates but with recurrent erosive and crusted lesions on the feet These again cleared completely with wet dressings of buffered cysteine hydrochloride solution

In October 1944 the patient returned, showing regrowth of all the nails to about one half of their original thickness As it was realized that the only method of completely stopping the growth of the nail would mean complete removal of the matrix, which in the condition is apparently the root from which

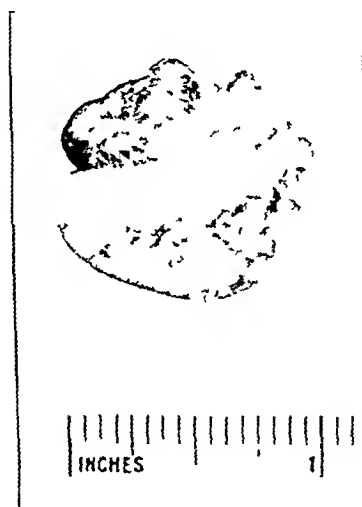


Fig 4—One of the removed finger tips, showing the upward growth of the nail

the nail grows, it was decided in consultation with Dr Rosemond to remove completely the tip of one finger as a trial method of therapeusis Obviously such a procedure would result in a finger completely lacking a nail

The next admission to the hospital was in February 1945, and this time the boy requested that the same procedure of removing the distal phalanges be used for all the fingers and the thumb of the right hand, as he had had no discomfort in the one finger and could use it for the first time in his life The operation was performed with the patient under general anesthesia In June 1945 the same procedure was followed with the left hand, the operation having been almost completely successful on the right hand Apparently a small amount of matrix was not removed from the middle finger, and it resulted in a slight regrowth of the nail The final result of the operations may be seen in figure 5 Microscopic study of the distal phalanges, including the structure of the nails, was impossible

6 Goldberg, L C Resistant Erosive Lesions in Pachyonychia Congenita of Jadassohn Treatment with Buffered Cysteine Hydrochloride, Arch Dermat & Syph 36:331-334 (Aug) 1937

because of lack of a satisfactory method of softening the nail sufficiently to permit cutting with the microtome

A biopsy of tissue from one of the crusted inflammatory denuded patches resulted in the following report "The tissue consists of an outer thick layer of keratin material which has a laminated appearance. It contains numerous pyknotic nuclei. Below this is a layer of stratified squamous epithelium which is moderately acanthotic. It has a pseudopapillary arrangement. Its rete pegs are disorderly. The corium shows fibrous thickening and adenomatoid hyperplasia. The histologic picture could be that of a clavus or pachyderma."

The second case has not been studied as intensively, nor has it been possible to keep the patient under as close observation as the patient in case 1, but it is included chiefly because of the extreme early age at which the patient was first seen.

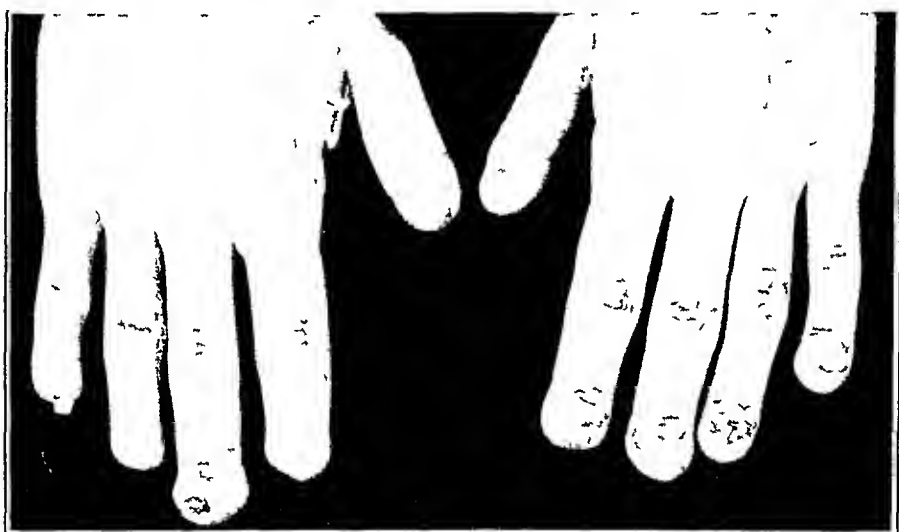


Fig. 5—Appearance of the hands one year after removal of distal phalanges

CASE 2—T. N., a 5 month old infant girl, was seen in consultation in February 1942. The entire skin was dry, with some papular accentuation of the follicles, particularly on the extensor surfaces. On the trunk were two small irregular hemangiomas of the strawberry mark type. The nails were all greatly thickened, with the excessive growth away from the nail matrix rather than away from the tip of the nail plate. The mucous membranes showed several superficial white patches, which had been diagnosed and treated by a pediatrician as "thrush." The case was presented to the Philadelphia Dermatological Society as a typical case of pachyonychia congenita. Treatment consisted in (1) application of solid carbon dioxide to the nevi, (2) administration of massive doses of vitamin A and (3) local application of a mild emolient.

#### COMMENT

In addition to adding 2 cases of this rare congenital anomaly to the literature, our interest was directed to the question of therapy. There are three phases of pachyonychia congenita that distress the affected

person (1) the dry hyperkeratotic skin with acneform follicular keratoses, (2) the bullous and crusted lesions that appear from time to time, chiefly on the feet, and (3) the greatly thickened nails

We found that the dry skin could be kept in a comfortable state by massive doses (100,000 units daily or more) of vitamin A, infrequent bathing and the use of an emollient

At the Harriet Lane Hospital for Invalid Children (Johns Hopkins Hospital) the bullous and crusted lesions in case 1 were reported to have healed after treatment with compresses of chlorazodin, potassium permanganate dressings and gentian violet medicinal. It was not made clear which of these agents had proved most effective. At the Temple University Hospital various local applications were employed, including boric acid solution, wet dressings and a modified ichthammol ointment, but until wet dressings of a buffered solution of cysteine hydrochloride, as suggested by Goldberg,<sup>6</sup> were employed the results were discouraging. As described in case 1 the latter solution invariably healed the open lesions in from ten days to two weeks. Recurrence within a few weeks after application of the cysteine hydrochloride dressings was stopped was invariably the rule.

The cause of the greatest discomfort to the boy described in case 1 was the dystrophic finger nails, which rendered his fingers virtually useless. Removal of the nail plates proved ineffective, as regrowth was rapid. This is similar to Andrews'<sup>5</sup> experience, for in a case reported by him removal of the nails by a surgeon was followed by "regrowth in a distorted fashion."

Careful study of the growth of the nails in pachyonychia congenita indicates that growth is away from the matrix of the nail rather than from the root of the nail. Thus the only successful therapy consists in complete removal not only of the plate but of the matrix as well, which in these cases is identical with the root or origin of growth. Complete removal of the distal phalanges of the fingers and thumbs in 1 of our cases resulted in giving the patient useful fingers. This is forcefully illustrated by the fact that he is now taking piano lessons and has free use of the fingers in spite of the radical surgical procedure.

#### SUMMARY

1 Two cases of pachyonychia congenita are reported with clinical and laboratory findings

2 Studies of therapy indicate that (a) the dry keratotic skin may be improved by massive doses of vitamin A and emollients, (b) the use of wet dressings of buffered cysteine hydrochloride, as suggested by Goldberg, will temporarily heal the bullous and crusted lesions, and (c) removal of the distal phalanges of the digits is the only way to free the fingers of the distorted dystrophic nails and make them useful

## ABSTRACT OF DISCUSSION

DR HAROLD COFF, Cleveland The patient in the original case of Jadassohn and Lewandowsky was a girl 15 years old, and she had a brother aged 4 Her nails were thick and folded longitudinally and assumed a conelike surface, such as is shown in these pictures, while the great toe nails assumed somewhat the character of onychogryposis, which is well brought out in this boy The girl had hyperhidrosis of the nose, and there were patches of reddish papules on the nose with fine watery blisters In the summer the girl had bullous lesions on the soles, just exactly the same as this patient had, while both she and her brother had over the knees and elbows millet seed-sized papules, capped with a horny center, which on removal left a bleeding spot, this shows up well on this patient The patient also had lesions over the scapulas on the anterior and posterior axillary folds that were similar to this The tongue of the girl showed extensive leukokeratosis but not leukoplakia The tissues were really piled up There is a distinction

Kumer and Loos (*Wien klin Wchschr* 48 174, 1935) attempted to assemble some of these related dermatoses In one form there was a symmetric volar dermatosis with follicular keratoses of the body, in the second, there were keratoses of the hands or feet or both with leukokeratoses of the mouth and even of the vocal cords, i e, the so-called Riehl type, and third, there were the aforementioned changes along with the corneal alteration The process is dominant and is hereditary Some of the patients have the loss of hair, hyperhidrosis, formation of bullae and onychogryposis

The condition in the male patient seen by Rauschkolb, Toomey and Cole (*ARCH DERMAT & SYPH* 27 71 [Jan] 1930) and a counterpart more recently reported from Fred Wise's service by Garb and Rubin differed from pachyonychia congenita in that there was a dystrophy of the nails In our case the patient has a true leukokeratosis in the mouth but no involvement of the larynx

I was much interested in this report, and these cases certainly are extremely similar, outside of the dystrophy of the nails in the one instance as compared with the pachyonychia congenita that Jadassohn names in the other condition

DR FRED WISE, New York Two brothers with pachyonychia congenita treated by Dr Garb at the Skin and Cancer Unit of the New York Post-Graduate Medical School Hospital with testosterone propionate showed considerable improvement One of the brothers suffered from advanced leukokeratosis of the tongue and buccal mucosa, dystrophy of the nails, alopecia and hyperpigmentation of the neck and face, together with signs of hormonal deficiencies The leukokeratosis responded favorably but showed a tendency toward recurrence when the medication was discontinued Gain in weight and improvement of the general health of the patient were notable while the treatment was administered regularly

DR HAMILTON MONTGOMERY, Rochester, Minn Dr Ormsby and I have had difficulty in trying to group and classify some of these congenital ectodermal and mesodermal defects, and, in connection with the cases that Dr Cole mentioned that he has reported, I should like to call attention to an article by Dr Thannhauser on "Werner's Syndrome (Progeria of the Adult) and Rothmund's Syndrome Two Types of Closely Related Heredofamilial Atrophic Dermatoses with Juvenile Cataracts and Endocrine Features" (*Ann Int Med* 23 559-626, 1945) I believe that there are too many names for varying diseases that are related, and I hope that some one will straighten out this subject It is true that there are typical cases of pachyonychia congenita, and I do not question the diagnosis as presented

DR JOHN G DOWNING, Boston Dr Wise's remarks prompt me to describe a patient whom I saw June 24, 1944, a boy aged 16 years with a more or less generalized cutaneous disturbance. He had keratotic papules on his arms, legs and body, with bullous lesions on the hands and feet. There were paronychial lesions on most of the fingers, with changes in the nails consisting of ridges and subungual hyperkeratosis. I thought that he had a vitamin A deficiency, but he showed little improvement with large doses of vitamin A. He was later seen by an endocrinologist, who prescribed androgens 29 mg, a total of 17-keto steroids per twenty-four hours, and estrogens 36 mg, a total of 17-keto steroids per twenty-four hours. Under this therapy his cutaneous lesions were relieved, and at the last report, three months ago, he was still well.

DR CARROLL S WRIGHT, Philadelphia I appreciate the discussions. I really do not think that there is anything more that I can add. I agree that there is a great deal of confusion about this subject, but, if any one takes the trouble to look up the reported cases of pachyonychia congenita with which there are photographs, it will be seen that they all look just like this case, I think that this is a distinct type of congenital defect which probably deserves the term that it has been given.

## LONGITUDINAL GROOVING OF THE NAILS CAUSED BY SYNOVIAL LESIONS

C RUSSELL ANDERSON, M D  
BEVERLY HILLS, CALIF

**I**N 1942 Eliassow and Frank<sup>1</sup> contributed an excellent review of the literature on synovial lesions of the skin. They also demonstrated incontrovertibly the connection of the synovial lesions with adjacent joint cavities by aspirating a synovial lesion and then replacing the aspirated fluid with diodrast (Winthrop Chemical Company, Inc., 3, 5-diiodo-4-pyridone-N-acetic acid and diethanolamine [35 per cent weight per volume]). The roentgenogram taken immediately after the injection showed the contrast medium in the synovial lesion and in the adjacent joint itself. The authors offered the concept that synovial lesions of the skin were due to an escape of synovial fluid from the joint cavity.

The genesis of synovial lesions has never been satisfactorily explained. Ormsby<sup>2</sup> suggested an arthritic diathesis. Jensen<sup>3</sup> offered the concept that the synovial lesions had "their origin in embryonic arrests in the process of the development of periarticular tissue and synovial membranes." In 1937 Gross<sup>4</sup> stated his belief that the synovial cysts were the result of a peculiar mucoid degenerative change in the connective tissue of the corium, leading to liquefaction and cyst formation, and considered local injuries and thrombosis of small arterial channels as likely causes of this degeneration. I believe that synovial lesions appear as degenerative manifestations of the latter half of life, inasmuch as I have always seen them associated with some degree of hypertrophic arthritis of the terminal interphalangeal joints and never before the age of 40.

During the past ten years I have seen a large number of synovial lesions, but not until the past year have I seen a peculiar longitudinal grooving of the nails due to these synovial lesions, nor have I found it described anywhere. Fordyce<sup>5</sup> reported 3 cases in which cysts were present on the terminal phalanges of the fingers near the base of the nail,

1 Eliassow, A., and Frank, S. B. Pathogenesis of Synovial Lesions of the Skin. *Arch Dermat & Syph* **46** 691 (Nov) 1942

2 Ormsby, O. S. Synovial Lesions of the Skin, *J Cutan Dis* **31** 943, 1913

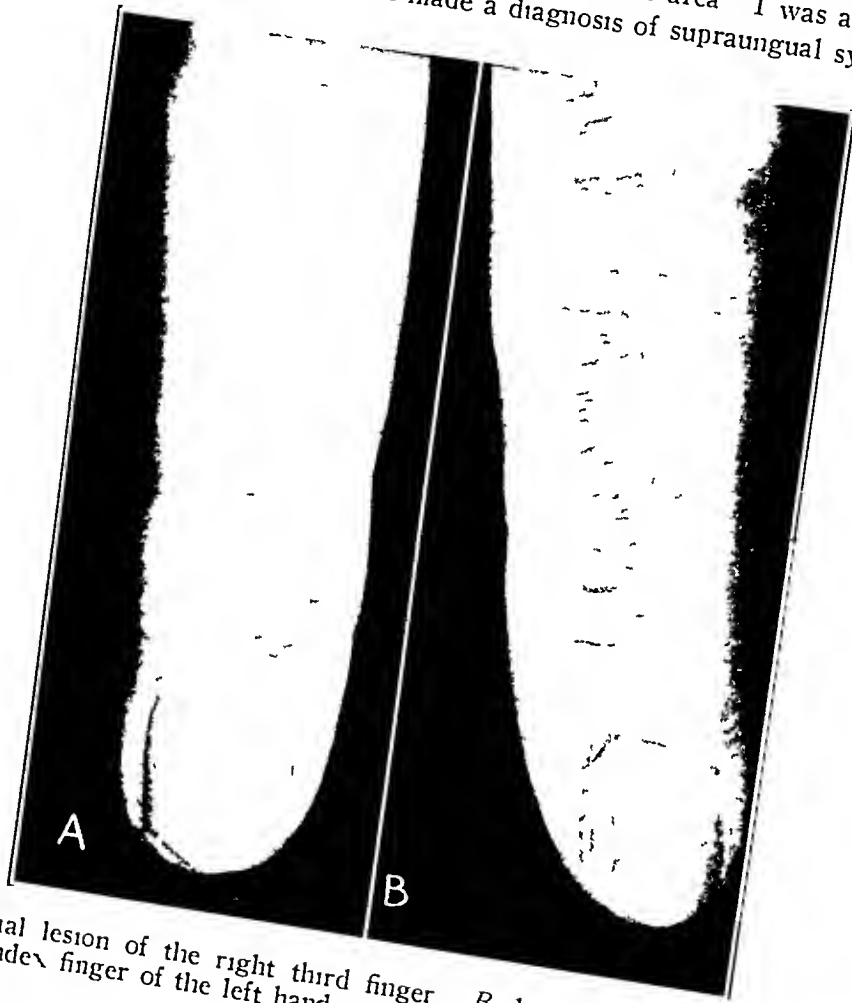
3 Jensen, D. R. Ganglia and Synovial Cysts. Their Pathogenesis and Treatment, *Ann Surg* **105** 592 (April) 1937

4 Gross, R. E. Recurring Myxomatous, Cutaneous Cysts of the Fingers and Toes, *Surg, Gynec & Obst* **65** 289 (Sept) 1937

5 Fordyce, J. A. Nail Cysts, *J Cutan Dis* **36** 589 (Dec) 1918

but he did not describe any changes in the nails. In his book, Pardo-Castello<sup>6</sup> referred to Fordyce's article but did not mention changes in the nails secondary to synovial lesions.

My first patient presented a lateral longitudinal grooving of the nail on the fifth finger of the left hand, without any evidence of cyst formation but with a complaint of tenderness of the nail root just proximal to the grooving of the nail. After three weeks she returned and told me that a small amount of clear viscid fluid had been expressed from under the fold of the nail near the longitudinal grooving, giving relief from tenderness of this area. I was able to express a small amount of this fluid, and I made a diagnosis of supraungual synovial lesion.



*A*, synovial lesion of the right third finger. *B*, longitudinal grooving of the nail on the index finger of the left hand.

My second patient presented a synovial lesion of the dorsal surface of the distal interphalangeal joint of the third finger of the right hand (fig. *A*) and a longitudinal grooving of the radial side of the nail on the index finger of the left hand (fig. *B*), both lesions having been present for six months. At this time there was no visible evidence of a synovial lesion associated with the longitudinal grooving of the nail, but the patient did complain of a slight degree of tenderness on pressure over the adjacent fold of the nail. Two weeks later there was a sudden increase of tenderness, and a tense swelling of the skin appeared over

<sup>6</sup> Pardo-Castello, V. *Diseases of the Nails*, ed 2, Springfield, Ill., Charles C Thomas, Publisher, 1941, p 58.

the root of the nail on the index finger of the left hand, just proximal to the grooving, as shown in the illustration (fig, *B*) After appropriate roentgen therapy, this cyst disappeared and the nail recovered its former normal contour I have seen several other similar cases

The diagnosis is simple when there is visible evidence of a cystic lesion on the same or other fingers However, this longitudinal grooving of the nail may be present for as long as six months before a visible associated cystic lesion appears Its presence in a person over 40 years of age should lead one to consider the existence of a synovial lesion lying over the nail root and disturbing the growth of the nail

#### SUMMARY

Longitudinal grooving of the nail plate due to the presence of a supraungual synovial lesion in the region of the nail root is described for the first time The genesis of synovial lesions is discussed

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## News and Comment

### GENERAL NEWS

**Rocky Mountain Dermatologic Society Formed**—On Jan 31, 1947 a group of dermatologists practicing in the Rocky Mountain region met in Denver for the purpose of discussing the formation of a dermatologic society for that region. The dermatologists in Denver had met at a previous date, establishing a temporary organization to prepare plans for the initial meeting.

The meeting began with the presentation of cases at the University of Colorado School of Medicine and Hospitals. Following the clinical portion of the meeting, a business session was held. The expressions of those gathered unanimously favored the formation of such a society for this area. A permanent organization was established, a constitution adopted, officers elected and the name Rocky Mountain Dermatologic Society accepted. Meetings will be held at least twice yearly. There are eighteen charter members, practicing in Denver, Colorado Springs, Colo., Pueblo, Colo., Salt Lake City and Albuquerque, N. M.

**American Board of Dermatology and Syphilology**—At the meeting of the American Board of Dermatology and Syphilology, Inc., in New York, April 25, 26 and 27, 1947, the following thirty-eight candidates were voted certificates, and they may now be referred to as certified specialists: Harold E. Anderson, Long Beach, Calif.; Paul Prince Boswell, Chicago; William Cohen, Trenton, N. J.; Charles J. Courville, Detroit; Will Charles Davis, Portland, Ore.; David J. Dolan, Brooklyn; Lemuel Price Ereaux, Montreal, Canada; Benjamin David Erger, Brooklyn; Alfred B. Falk, Chicago; Merriam G. Fredericks, Duluth, Minn.; Abraham J. Gewirtz, Brooklyn; Alexander Gregor Gradow, San Francisco; Meyer Hantman, Cleveland Heights, Ohio; Joseph M. Hitch, Raleigh, N. C.; William McPherson Huber, New York; David Kahn, Lansing, Mich.; William Henry Kaufman, Charlottesville, Va.; Joseph V. Kennedy, Washington, D. C.; Charles Walter Knerler, Oklahoma City; Max Elliott Krause, Oakland, Calif.; Georges Leclerc, Montreal, Canada; Morris Leider, Brooklyn; Milton E. Lowell, Westfield, N. J.; Columbus Hal McCuiston, Austin, Texas; James A. McGuire, Denver; Frederick R. Mebel, Rockville Center, Long Island, N. Y.; Rafael Rivera, New York; Walter Felix Rosenberg, Hempstead, Long Island, N. Y.; Gdali Rubin, Brooklyn; David Mitchell Sidlick, Philadelphia; John Clark Slaughter Jr., Ann Arbor, Mich.; Harry R. Staley, Kansas City, Mo.; Howard Paul Steiger, Philadelphia; Gustav Weissberg, New York; John Francis Wilson, Philadelphia; Eliot Wolf, Studio City, Calif.; George Joseph Zippin, New York; and Isadore Zugerman, Philadelphia.

The following eight candidates were also successful in the examinations and will become certified specialists when they have fulfilled the requirement of five years of training and experience in the specialty: Edward Hunter Boggs, Charleston, W. Va.; Marcus B. Einhorn, Albany, N. Y.; Zachary Felsner, Chicago; Phyllis E. Jones, Oklahoma City; Rose B. Saperstem, New York; Arthur Louis Shapiro, Chicago; Evelyn G. Wallace, Hot Springs, Ark.; and Herschel Selig Zackheim, Detroit.

## Abstracts from Current Literature

### STEVENS-JOHNSON SYNDROME (ERUPTIVE FEVER WITH STOMATITIS AND CONJUNCTIVITIS) SIMON KOVR, Am J M Sc **210** 611 (Nov) 1945

The author describes 2 cases of Stevens-Johnson syndrome, whose clinical course is characterized by the acute onset of fever and prostration, associated with a cutaneous eruption, severe membranous stomatitis and purulent conjunctivitis. A macular-papular or vesicular eruption, which varies in severity in individual cases, may be present. The course usually lasts about two to three weeks and may be followed by a recurrence. Though he states that "Certainly this syndrome differs from erythema exudativum multiforme," several of the excellent photographs represent eruptions which most dermatologists would readily diagnose as erythema multiforme. Thus there remains some question whether the titles "Stevens-Johnson syndrome" or "eruptive fever with stomatitis and ophthalmia" are any more suitable than erythema multiforme.

### INFECTIOUS MONONUCLEOSIS. AN ANALYSIS OF 26 CLINICAL AND 340 SUBCLINICAL CASES. RAY VANDER MEER, CHARLES H. LUTTERLOH and JEAN PILOT, Am J M Sc **210** 765 (Dec) 1945

The authors observed a series of 356 patients whom they thought had infectious mononucleosis. The study is of a broad nature, giving particular consideration to subclinical cases. Of greater dermatologic interest are the 18 typical cases in 8 of which (30 per cent) an eruption was present. In 2 of these it was practically indistinguishable from the typical rash seen in measles, and in a third it appeared more like the usual manifestation in early scarlet fever. It is noted that other observers have recorded purpuric, vesicular and urticarial eruptions and that some eruptions are practically indistinguishable from German measles.

### THE USE OF A HISTAMINE ANTAGONIST, BETA-DIMETHYLAMINOETHYL BENZHYDRYL ETHER HYDROCHLORIDE, IN ALLERGIC DISEASE. ALAN S. FRIEDLAENDER, Am J M Sc **212** 185 (Aug) 1946

Friedlaender reports on the results of use of Benadryl (beta dimethylaminoethyl benzhydryl ether hydrochloride) in a group of 47 patients with a variety of allergic complaints. Of the patients with urticaria all had some degree of relief, and Friedlaender regards the drug as the most effective agent yet used as a palliative measure. Of 4 patients with atopic eczema 2 had decided reduction of pruritus after taking the drug.

Sixteen of the 47 patients complained of some side effects following use of the drug. The commonest symptoms were drowsiness, dizziness, weakness, faintness, fatigue and gastrointestinal upsets.

### CAPILLARY MICROSCOPY, WITH SPECIAL REFERENCE TO CAPILLARY PETECHIAE. ELI DAVIS, Am J M Sc **212** 192 (Aug) 1946

Using a standard binocular microscope, Davis examined the finger nail beds of over 1,000 patients. He points out that the capillary pattern of any person is usually consistent. While variations are observed frequently, he states the belief that unwarranted inferences have been drawn from those variations which are well within normal. He states that he has not yet seen capillary petechiae in a healthy person, though many patients showed such lesions when no cutaneous petechiae were seen. No type of petechia was pathognomonic of any disease. One hundred patients with petechiae were found among 533 consecutive patients examined by capillary microscopy. Among these patients were 3 of 13 patients with syphilis and 4 of 7 patients with Raynaud's disease.

CLINICAL AND LABORATORY STUDIES OF LIVER FUNCTION IN THERAPEUTIC MALARIA  
PAUL M. GLENN, LAWRENCE I. KAPLAN, HILTON S. READ and FREDERIC T. BECKER, *Am J M Sc* **212** 197 (Aug) 1946

The authors report the results of investigation of a group of 60 patients inoculated with malaria. They conclude that the liver is involved in every case of malaria, showing some degree of dysfunction by various tests. In most instances the involvement is not severe, since the tests of hepatic function show a return to normal in a short period. The results of cephalin cholesterol flocculation test return to normal more slowly. Their patients were divided in three groups, depending on the diet and on the dietary supplements given. Clinical jaundice appeared about equally in all three groups. There was no correlation between the observation of jaundice and the palpability of the liver. Enlargement of the liver was found less frequently among patients who were given 75 Gm of dextrose intravenously daily. Tests of hepatic function failed to show any protection of the liver by the addition of protein to the diet, high vitamin intake or injections of crude liver extract. The authors conclude that the digestive symptoms experienced during malaria therapy are not dependent on the hepatic disease but largely on the malaria and perhaps the fever itself.

AN ACCOUNT OF STOCK REGINALD FITZ, *Arch Int Med* **76** 210 (Oct) 1945

Many physicians have expressed the opinion that there has developed in the medical profession an ominous liability to coronary thrombosis or other manifestation of vascular disease. Fitz has studied the problem by investigating the obituary columns of *The Journal of the American Medical Association* and comparing the data with several statistical surveys, arriving at several interesting conclusions. Year by year, fewer physicians under 60 years of age are dying, and more are living to attain 70 and 80 year marks since the total number of physicians living to pass the age of 60 has increased steadily. Vascular disease is now encountered commonly as a cause of death among physicians at all ages and is increasing in frequency.

There has been a satisfactory diminution in the relative number of deaths from all causes and among all ages, especially notable among those under 40 but perceptible among those over 60. Physicians differ little from the rest of the citizens of the United States in respect to the causes of their deaths at different ages though physicians up to the age of 60 are somewhat protected as a class, considerably few of them, for example, die of accidents and tuberculosis and their specific death rate from all causes is lower. Physicians past 50 appear to have proportionately more fatal cerebral vascular accidents and a slightly higher death rate from all causes. If deaths from cardiac, renal and cerebral vascular disease are grouped, physicians between 40 and 60 years of age appear to die a little more commonly from these causes than do members of the general white male population, probably because they have a better chance of avoiding death from other insults. Fitz concludes that so long as physicians continue to improve their methods and to build up a profession whose members grow steadily older in years and larger in numbers, the mortality rate from vascular disease will increase.

SICKLE CELL ANEMIA IN WHITE PATIENTS WITH ULCERS OF THE ANKLES. REPORT OF TWO CASES. A. C. WOOFER, WILLIAM S. DICK and WALTER L. BIERRING, *Arch Int Med* **76** 230 (Oct) 1945

Quoting authoritative reports, Woofter, Dick and Bierring state that sickle cell anemia can occur in white persons. They describe a family without known negroid influences but with a brother and sister having characteristic anemia and ulcers of the ankles. Their grandmother had pallor and ulcers of the ankles, a father and uncle were pale and had recurrent ulcerations since childhood, one brother had delayed sickling and another brother was apparently normal.

TUMOR OF TACTILE END ORGANS JAN CAMMERMEYER, Arch Path **42** 1 (July) 1946

Cammermeyer describes an unusual tumor which contained well developed tactile corpuscles but did not give any subjective sensation to the patient. It contained multiple tactile end organs or corpuscles and showed great variations in the number of nerves, their course and their caliber. The specific portion of the tumor was surrounded by a mass of connective tissue. The author states the belief that the tumor may have developed because of faulty organization of embryonal tissue, as has been theorized in the case of other neurogenic tumors.

ANGIOMATOID FORMATIONS IN THE GENITAL ORGANS WITH AND WITHOUT TUMOR FORMATION ROBERT P. MOREHEAD, Arch Path **42** 56 (July) 1946

Morehead points out that in recent years a group of neoplasms have been noted in the genital tract which possess an unusual but characteristic morphologic picture. He points out that the lesions under consideration are composed primarily of two structural units, namely (1) fibromuscular tissue of the type which ordinarily composes myoma and (2) groups of cells which are predominantly angiomatoid in arrangement and are intermingled with cells structurally resembling small lymphocytes. After studying the available cases he expresses the opinion that the data strongly support the hypothesis that angiomatoid tissue is derived from mesenchymal cells which make imperfect attempts at the formation of lymph vessels and lymphocytes.

HEPAR LOBATUM CLINICAL SIGNIFICANCE OF THE ANATOMIC CHANGES DOUGLAS SYMMERS and DAVID M. SPAIN, Arch Path **42** 64 (July) 1946

The authors state that over a period of thirty years hepar lobatum was encountered 102 times among 23,792 necropsies at Bellevue Hospital. According to the clinical records of 28 cases that were available for analysis, the lesion occurred 23 times in men and 5 times in women, 24 patients were of the white race and 4 were Negroes. The average age was 38.5 years, the youngest patient was 19 and the oldest 80. Six patients admitted excessive use of alcohol. The diagnosis of syphilitic cirrhosis of the liver was made during life in 3 cases, and the disease was suspected in 1. Clinical records were available for analysis in 28 cases, in only 4 of which had the diagnosis been suspected or made during life. In most instances the liver was palpable, and in half the cases the spleen was palpable. Jaundice occurred in 8 cases, ascites in 18 and hematemesis in 7. An irregular temperature was present in 12 cases. Symmers and Spain state that the clinical diagnosis of hepar lobatum is dependent almost exclusively on physical signs rather than symptoms. They express the opinion that in attempting a clinical diagnosis confirmatory evidence should be sought in the form of response to treatment and consideration should be given to the advisability of biopsy.

BIREFRINGENCE IN TISSUES A. L. LICHTMAN and JOHN R. McDONALD, Arch Path **42** 69 (July) 1946

Double refraction of light by biologic substances is a reflection of the fundamental structure of tissues. Three types of birefringence in tissues have previously been described. The author briefly discusses the changes which have been observed in hair, nail and horn. He also points out that microscopy with polarized light aids in distinguishing between granulomas produced by bacteria and those produced by viruses. He also notes that study of the cholesterol esters aids in the interpretation of various inflammatory processes. He expresses the belief that further benefits are to be gained by the use of the polarizing microscope in pathology.

TREATMENT OF POST-TRAUMATIC SIMMONDS' DISEASE WITH METHYL TESTOSTERONE LINGUETS H. LISSER and L. E. CURTIS, J Clin Endocrinol **5** 363 (Nov) 1945

Lisser and Curtis describe a 20 year old man whose panhypopituitarism followed fracture of the skull. Among the signs of the disease were progressive loss of

facial and body hair (the scalp hair remained normal), loss of libido and potentia, increasing fatigability, and the skin acquired a fawn color. In the course of nine months' treatment with methyl testosterone linguets, the sexual hair reappeared and there was general recovery.

CHRONIC IDIOPATHIC HYPOPARATHYROIDISM WITH SUPERIMPOSED ADDISON'S DISEASE IN A CHILD MARTHA F LEONARD, *J Clin Endocrinol* 6:493 (July) 1946

ADENOCORTICAL CANCER WITH UNDULATING FEVER IN ADDISON'S DISEASE A P CAWADIAS, *ibid* 6:507 (July) 1946

ADDISON'S DISEASE IN AN INFANT J C JAUDON, *ibid* 6:558 (Aug) 1946

These individual reports are of interest because they do not describe the usual aspects of Addison's disease. Leonard reports the rare occurrence of combined parathyroid and adrenal insufficiency. The hypoparathyroidism began at about 3 years, and the Addisonian pigmentation appeared at about 10 years. Necropsy established almost complete absence of adrenocortical tissue and no demonstrable parathyroid tissue.

Cawadiaz reports an instance of Addison's disease caused by adrenocortical carcinoma, and he expresses the opinion that this association may not be so rare as is generally thought. The author also gives consideration to the presence of fever and to psychologic manifestations in Addison's disease.

Jaudon reports an instance in which Addison's disease began in the first year of life and followed the usual course. In this case it was thought that tuberculosis was the etiologic agent responsible for hypofunction of the adrenal cortex.

LYNCH, St Paul

LICHENOID DERMATITIS EUGENE S BERESTON, *J Invest Dermat* 7:69 (April) 1946

The author presents his observation of 200 cases of so-called lichenoid dermatitis, a chronic dermatosis which occurred among personnel stationed in the South Pacific area and other areas where quinacrine hydrochloride was administered in relatively large amounts over long periods.

Three distinct clinical types of lesions were observed. The eczematoid type was the commonest and usually involved the dorsal surfaces of the extremities. The lichen planus-like type often involved the entire body, including the mucous membranes. The mixed type consisted of eczematoid and lichen planus-like lesions occurring in the same person. All three types often changed into an exfoliative dermatitis of serious proportions.

The histopathologic picture chiefly resembled that in lichen planus, although some characteristics of psoriasis were also present.

The prognosis for cure of the acute lesions is excellent provided the patient is evacuated from the tropics.

A COMBINATION TREATMENT FOR LICF AND SCABIES GAINES W EDDY, *J Invest Dermat* 7:85 (April) 1946

The author, a member of the Department of Agriculture, presents a formula designated as N B I N, consisting of benzyl benzoate (68 parts), Tween 80 (14 parts), benzocaine (12 parts) and DDT (dichlorodiphenyltrichloroethane) (6 parts), for the treatment of pediculosis capitis, Phthirus pubis and scabies.

It is claimed that this formula is nontoxic and nonirritating, can be applied safely to the more tender areas of the body and is highly effective not only against the parasites but also against their eggs.

SCABIES AND PEDICULOSIS TREATED WITH BENZYL BENZOATE, D D T BENZOCAINE EMULSION CIDRIC C CARPENTER, JOHN A HEINLEIN, MARION B SULZBERGER and RUDOLF L BAER, *J Invest Dermat* 7 93 (April) 1946

An analysis is presented of the various methods for the treatment of scabies used at the United States Naval Hospital, Brooklyn —

The sulfur treatment required an average hospitalization period of ten days and produced a high incidence of secondary dermatitis

The treatment with benzyl benzoate was found to be an improvement over all former methods and reduced the patients' stay in the hospital to five and one-half days. The incidence of irritations was less frequent provided the treatment could be limited to one or two applications

The formula N B I N (benzyl benzoate, DDT and benzocaine emulsion) was found so satisfactory that no hospitalization was required, and one to four sprayings produced permanent cures in 41 of 42 patients. A single application was also effective in curing 15 patients with pediculosis pubis and 4 patients with pediculosis capitis

Although no evidence of toxicity developed in this series from N B I N the authors warn that further studies are required to confirm the lack of toxicity of DDT (dichlorodiphenyltrichloroethane) present in this formula

STUDIES IN HYPERSENSITIVITY TO LIGHT HAROLD F BLUM, RUDOLF L BAER and MARION B SULZBERGER, *J Invest Dermat* 7 99 (April) 1946

Studies on wavelength in a case of urticaria solaris showed that lesions were produced by wavelengths shorter than 3,700 angstrom units. The authors suggest that this condition be designated as urticaria solaris (wavelength less than 3,700 angstrom units) and should be regarded as a distinct etiologic entity

Through passive transfer tests photosensitivity was induced by the same wavelength in normal skin. It is suggested, since this syndrome has several causes and since each different spectral sensitivity represents a different light-absorbing substance, that wavelength limits should be established in all cases available for study

URTICARIA SOLARE (4000-5000A) HAROLD F BLUM, E E BARKSDALE and H G GREEN, *J Invest Dermat* 7 109 (April) 1946

Spectral studies in a case of urticaria solaris in which the patient was exposed to sunlight through corning glass filters revealed that the urticaria was produced by blue and violet light with wavelengths of 4,500 to 5,000 angstrom units

The authors feel that this type of urticaria is a distinct etiologic entity and is best described as urticaria solaris (wavelength 4,000 to 5,000 angstrom units). This eruption differs from a type of urticaria solaris produced by other wavelengths by the failure of passive transfer

DICHLORMAPHARSEN IN THE TREATMENT OF SYPHILIS GIRSCH D ASTRACHAN *J Invest Dermat* 7 117 (April) 1946

The author concludes, after the administration of four thousand, three hundred and sixty-six injections, that dichlorophenarsine hydrochloride appears to be an efficacious antisyphilitic drug. Primary, secondary and tertiary lesions healed promptly

The serologic reaction of the blood improved in 64.8 per cent of the cases of late latent syphilis, in 100 per cent of the cases of early latent syphilis and 70 per cent of the cases of tertiary syphilis. The serologic reaction in cases of early syphilis changed to negative after 206 injections given once or twice weekly and 246 injections with the Eagle-Hogan method

Toxic reactions, in general, were few, and no cases of exfoliative dermatitis, encephalitis or jaundice were encountered in this series

Dichlorophenarsine hydrochloride was found to be less toxic but also less potent than oxophenarsine hydrochloride

## PINTA-LIKE LESIONS AMONG NATIVES OF GUAM RALPH F ALLFN and RAYMOND H GOODALE, U S Nav M Bull 46 653 (May) 1946

A recent survey of approximately 2,000 natives on Guam revealed 39 with hyperpigmentation and depigmentation of the skin, the lesions being limited to the extremities and the face. A high percentage yielded positive serologic reactions of the blood, although careful examination and questioning failed to reveal any evidence of yaws or syphilis.

This disease is known to the natives as "peladang" and is more prevalent in the southern half of the island, where rainfall is abundant and the relative humidity is high.

History indicates that the lesions usually appear as a small hyperpigmented area on the dorsum of the hands or feet, accompanied with mild itching of one week's duration. These areas spread slowly, and other darkened areas appear nearby and on other extremities. As the lesions increase in size the centers become depigmented, enlarge and coalesce to produce large grayish to white areas of irregular shape. No constitutional symptoms are attributed to the disease.

Observation of the fully developed condition revealed irregular-shaped areas of hyperpigmentation interspersed with depigmentation. Depigmented areas varied from grayish white to a pinkish hue, and often the alteration of pigment was symmetric in distribution.

Histopathologic examinations failed to reveal specific characteristics except for the lack of pigment in the basal cell layer from the specimens taken from depigmented areas and the abundance of pigment in the basal layer from the specimens taken from hyperpigmented areas.

Dark field examinations failed to reveal spirochetes, although the Kahn reactions of the blood were positive in all cases.

One patient who received antisyphilitic treatment on the basis of a positive reaction of the blood noted a regression of all hyperpigmented lesions. At the time of examination, only grayish areas of depigmentation were noted and the Kahn reaction of the blood was still positive.

The authors express the opinion that these cases occupy the same position among the treponematoses as pinta does in the Western Hemisphere.

## CUTANEOUS DIPHTHERIA JACK V CHAMBERS, U S Nav M Bull 46 744 (May) 1946

A case of cutaneous diphtheria is reported in which the condition originated as a blister on a lower extremity. Examination a year after onset revealed a large round ulcer, with raised rolled edges of a bluish tinge, covered with a hard leathery scab. Smears and cultures revealed *Corynebacterium diphtheriae*. The fermentation reaction likewise was characteristic for this organism. Results of treatment with intermuscular and local application of diphtheria antitoxin were unsuccessful at the end of seventeen days. The ulcer healed rapidly after the injection of 600,000 units of penicillin over a six day period in conjunction with topical compresses.

The author suggests that antitoxin should always be administered, in spite of its failure to produce a cure, in order to counteract possible paralysis.

## OBSERVATIONS AND DATA ON PREVENTION OF POISON-OAK DERMATITIS GEORGE G NOVACOVICH, U S Nav M Bull 46 811 (June) 1946

Poison oak dermatitis constituted one of the major causes for time lost from training at Preflight School, St Mary's College, California. Consequently, studies were made to determine the best methods for hyposensitization and topical protection.

Hyposensitization to the ivy resin was best achieved by the use of large doses of antigens administered orally according to the recommendations of Shelmire.

Topical protection was best afforded by 10 per cent chlorinated lime ointment and Navy antigas protective ointment, through destruction or inactivation of the ivy resin. No protection was afforded by zinc oxide ointment, 10 per cent sodium perborate ointment or urea peroxide.

COMPARATIVE EVALUATION OF PREPARATIONS FOR THE PROPHYLAXIS AND TREATMENT OF FUNGOUS INFECTIONS OF FEET MARION B SULZBERGER and ABRAM KANOF, U S Nav M Bull 46 822 (June) 1946

This study adds further data to a previous report on antifungous agents and provides additional information on the efficacy of calcium and zinc propionate powder, diodoquin powder, vioform powder, talcum powder, U S N foot powder and thiourea powder in the prophylaxis of fungous infections of the feet.

Previous findings were confirmed that undecylenic powder was the most effective, practical and acceptable agent for prophylactic use in fungous infections of the feet. It was also superior in the maintenance of freedom from even minimal or "subclinical" evidences of infection. No significant differences in the efficacy of undecylenic powder or ointment were noted.

Experiments in which the patients kept their shoes and socks on continuously for seven days indicated that undecylenic powder was superior to diodoquin powder both prophylactically and in the treatment of mild infections.

DIAGNOSIS OF INFESTATION WITH "SARCOPTES SCABIEI" VAR "HOMINIS" EUGENE A HAND, U S Nav M Bull 46 834 (June) 1946

The purpose of this article is to popularize a little known method for making the diagnosis of scabies, particularly in an atypical condition. The technic of the slice, scrape and smear method is described in detail, and photomicrographs of an acarid, acarid eggs, hexapod larvae, skeletal parts of an acarid, scybala and acarid burrows are presented as an aid in identification. The life cycle of *Sarcoptes scabiei* var. *hominis* is presented.

TREATMENT OF INFECTED SEBACEOUS CYSTS JACK FISHMAN, U S Nav M Bull. 46 917 (June) 1946

A new method is described for the treatment of infected and noninfected sebaceous cysts. The technic consists in making a stab wound into the cyst, evacuating the contents and placing a small solid piece of silver nitrate into the cavity. In about twenty-four hours the wall of the cyst becomes discolored, and it is removed from the surrounding tissue by a hand forceps. The cavity is allowed to heal by granulation. No recurrences or ill effects were noted in 512 cases observed over a period of one year.

RODIN, South Bend, Ind

DERMATOMYOSITIS AND MALIGNANT TUMOR A DOSTROVSKY and F SAGHER, Brit J Dermat 58 52 (March-April) 1946

The authors report 2 cases of dermatomyositis associated with malignant new growth. The patient in the first case was a woman aged 33 in whom a tumor of the left breast developed. This was followed, six months later, by edema telangiectases and atrophy of the skin which, at the start, offered the aspect of acute lupus erythematosus, accompanied with pain in the joints and muscles. After the tumor had metastasized, poikilodermal features became more distinct, with atrophy of the musculature. The patient died. A striking feature was the restriction of the dermatomuscular symptoms as well as the tumors to the upper part of the body.

The second patient was a woman aged 65 in whom the entire skin, particularly on the upper part of the body, showed pigmentation, swelling, atrophy and telangiectases. There was, in addition, swelling of the muscles, paresis, dysphagia and tenderness on pressure. Gynecologic examination was made, and there was found to be a tumor of the right ovary, probably malignant. Since active treatment was

out of the question because of the poor condition of the patient, she was discharged and could not be followed further. She died two months later, and no postmortem examination was done.

The authors conclude that there is a relationship between dermatomyositis and malignant tumors. The appearance of the dermatomuscular symptoms shortly after the development of the tumor and, moreover, their intensification on metastasizing of the tumor, thereafter persisting until the patient succumbed in a state of carcinomatous prostration, would uphold their views.

SCABIES NORVEGICA IN A NATIVE OF EAST AFRICA F. PIERS and G. L. TIMMS, *Brit J Dermat* 58:61 (March-April) 1946

The occurrence of Norwegian scabies in a native of East Africa seems to be sufficiently uncommon to justify a report.

The patient, a girl of 15 years, was one of those persons "among whom washing is indulged in with the utmost caution." The patient did not complain of itching. A widespread eruption was present, consisting of round, elevated papules, measuring from the size of a pea up to a diameter of more than 2 inches (5 cm). The areas chiefly affected were the trunk, umbilicus, lower part of the back, lateral aspects of the abdomen and thighs, buttocks, both elbows, knuckles of both hands and proximal parts of the fingers.

Histologically, in the epidermis were sections of *Sarcoptes* of both sexes and in all stages of development, including eggs.

BLUEFARB, Chicago

RADIUM TREATMENT OF CARCINOMA OF THE LIP A. A. CHARTERIS, *Brit M J* 1:719 (May 11) 1946

This report covers 246 patients with cancer of the lip treated at the National Radium Center, Western Infirmary, Glasgow, Scotland, from 1928 to 1944 inclusive. The primary lesion was found on the lower lip in all except 8, in whom it was on the upper lip. With 8 exceptions the patients were men, and in only 75 instances was there sufficient doubt about the diagnosis to require microscopic confirmation. Of the patients, 208 had no obvious involvement of glands at the time of primary treatment, and, although the neck was not dealt with, in only 19, or about 9 per cent, did cervical metastases develop at a later date. The policy therefore has been to treat the primary lesion only, the follow-up examinations being relied on to detect any evidence of glandular involvement. Both implantation of radium and double radium molds were utilized in treatment, the dose delivered being from 5,000 to 6,000 r. By careful measurement of the needle pattern and placing of the plane in the center of the thickness of the lip, undesirable effects can be almost completely eliminated. When the conditions were not complicated by glandular invasion, 165, or 94 per cent, out of a total of 175 patients were rendered free from disease. When involvement of the glands was present to begin with or developed at a later date, the picture was decidedly different, in that only 25, or 48 per cent, out of 53 patients were cured. Failure of cure represented death of the patient from cancer usually about a year from treatment. In all patients treated, with or without involvement of the glands and including those rejected as untreatable and those operated on satisfactorily, the rate of cure was 73 per cent. Tabular results show that implantation methods are superior to molds.

VARICELLA HERPETIFORMIS P. H. PETERSON and S. A. B. BLACK, *Brit M J* 1:762 (May 18) 1946

The authors describe 2 cases of chickenpox which followed exposure to patients with herpes zoster on an isolated island where conditions made it unlikely that any undetected cases of chickenpox could have existed. They questioned the advisability of isolating patients with herpes zoster.

SHAW, Chattanooga, Tenn.

# Society Transactions

## NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILOLOGY

Lewis B Robinson, M D , *Chairman*

Samuel M Peck, M D , *Secretary*

Oct 2, 1945

### Granuloma Inguinale Presented by DR FRANK C COMBES

M K , a Negro woman aged 55, with a past history of no significance, was admitted to the dermatologic service of Bellevue Hospital with an eruption of the groin and genital regions of five weeks' duration

There were quarter to silver dollar size, sharply demarcated, granulating areas in the right and left inguinal regions and on the base of the major labia of the vulva, accompanied with mild edema of the vulva The borders of the lesions were grayish white

Laboratory Studies A smear was positive for Donovan bodies The Wassermann reaction of the blood was negative Frei and Ducrey tests gave negative reactions The urine was normal The red blood cell count was 3,420,000, the hemoglobin content, 80 Gm per hundred cubic centimeters, and the white blood cell count 13,900, with 55 per cent polymorphonuclear leukocytes, 32 per cent lymphocytes, 9 per cent monocytes, 3 per cent eosinophils and 1 per cent basophils

Biopsy revealed a structure compatible with granuloma inguinale

Treatment has consisted of fuadin, 5 cc, administered intramuscularly three times weekly Six injections have been given to date

### Frambesiform Tertiary Syphilis Presented by DR FRANK C COMBES

M B , a Negro woman aged 55, was admitted to the dermatologic ward of Bellevue Hospital with a generalized eruption of one month's duration There is no history of previous genital sores, generalized eruption or previous injections for syphilis The patient has never left the United States, having lived in North Carolina all her life, traveling to and from New York city for the past twelve years The only past illness was pneumonia in 1937, at which time the blood test for syphilis gave a negative reaction

Examination reveals discrete and confluent crusted and ulcerating lesions affecting the face, scalp, back and all extremities, with relatively few lesions on the chest Some of the lesions are sharply demarcated from the normal skin, while others blend gradually with the surrounding tissue The floor of the lesions appears clean and granulating, with little purulent material

Laboratory Findings Dark field examination for spirochetes gave negative results The Wassermann reaction of the blood was 4 plus The urine was normal The red blood cell count was 4,920,000, the hemoglobin content, 11 Gm per hundred cubic centimeters, and the white blood cell count, 26,200, with 77 per cent polymorphonuclear leukocytes, 14 per cent lymphocytes and 9 per cent monocytes

Biopsy was reported to show "acute and chronic inflammatory reaction"

Treatment has consisted in injections of penicillin, 40,000 units every three hours

## DISCUSSION

DR HERMAN GOODMAN The entire face and much of the body were covered with crusts overlying pustules when the patient was first admitted to the ward. The ulcers appeared after thorough scrubbing and application of ointment. Several physicians from Central and South America discussed the possibilities of frambesia (yaws) and rupial syphilis. It is the opinion of many that this patient presents a form of syphilis with adherent crusts and that a good ablution will remove most of the superficial, superimposed layers of crust.

DR EUGENE T. BERNSTEIN From my experience in Russia during pre-revolutionary days, this form of syphilis is one occurring more frequently in subjects of cachexia, debauchery or extreme poverty. Syphilis frambesoides (frambesoid syphilis) is a syphilitid usually observed in the third year, less often in the second, and is composed of luxuriantly suppurative warty growths. When untreated it may present a generalized eruption. The course of this nodular lesion is indolent and resolution ensues by resorption, leaving livid, pigmented maculations at the site of the nodules. This rupioid eruption, I recall, was readily amenable to orthodox antisyphilitic therapy and did not present any therapeutic difficulties.

DR E. W. ABRAMOWITZ This type of syphilis is not common here. While dirt may account in part for the appearance of the lesions, I do not think it accounts for it entirely. It is due to the poor resistance of the patient. As to the question of yaws, the lesions should show an abundance of spirochetes in case of that disease, whereas there would be few or none in a syphilitic lesion in the tertiary stage.

DR HERMAN GOODMAN Are the terms frambesiform and rupial synonymous? The characteristic frambesiform syphilitid has two, three or, at most, four lesions, each with a strawberry-like protuberance beneath the removed crust. The strawberry protuberance is not unlike granulation tissue, and the causative *Treponema pertenue* is easily demonstrated.

DR EUGENE F. TRAUB Dr Goodman has covered most of the salient points, and I agree with him in the essentials. The widespread, generalized eruption presented by the patient does not conform to frambesiform syphilis as taught by Dr Udo J. Wile. It is unusual in frambesiform syphilis to have more than five or six lesions, and these lesions are most commonly scattered about the face, especially about the nose and ears. The character of the individual lesion, as has been stated, is relatively soft, fungating and suggestive of a raspberry, and not at all like an oyster shell, as are those seen in this patient. The lesions presented by Combes's patient are heaped-up crusts of varying sizes like the layers of an oyster shell, and represent a typical rupial syphilitid. This disease was not uncommon in the West and occurred most often in women, particularly in women with poor general health and nutrition. It was looked on as a malignant type of syphilis. I believe the important consideration in cases of this type is the lowered resistance and poor nourishment rather than filth, although poverty, filth and undernourishment of course go more or less hand in hand.

DR GIRSCH D. ASTRACHAN I think this case is one of rupioid syphilis. The disease is not a tertiary stage but belongs to the group of late secondary forms. These appear in improperly treated syphilitic patients or in those with a low resistance. I never saw a patient with lesions as extensive as this. I am surprised that the histologic picture does not show the characteristics of syphilis.

DR PAUL GROSS The multiplicity of lesions and the character of the eruption would favor the diagnosis of rupioid syphilis. In that case one would have to assume that the patient's disease is in the secondary stage. The presence of ulceration shows only the appropriateness of the term syphilis precox. One can find this type of eruption even in the early secondary stage and in the presence of the primary lesion. Precocious tertiarism also expresses itself in the absence of spirochetes in the lesions, even if they represent the early secondary stage. The name malignant syphilis applies as little to this condition as it does to endemic

syphilis, which is usually of the cutaneous type and is known to have much less tendency toward visceral and neural involvement

DR CHARLES S MILLER An eruption of this type may occur in the unclean, but it is not due to uncleanness. It is due to the histologic response elicited. Syphilis is essentially a reaction of the cutis. The epidermis may become involved secondarily. In frambesiform tertiary syphilis the cutis shows the usual syphilitic reaction, but there are pronounced changes in the epidermis and the horny zone. The epidermis shows an irregular acanthosis, elongated rete pegs, intercellular edema and notable hyperkeratosis with some areas of crusting.

DR MAURICE J COSTELLO I agree with the discussers who believe that the disease is tertiary syphilis. The generalization of the eruption is in favor of the diagnosis of secondary syphilis, although the destructive process, which will terminate in scar formation, is in favor of the tertiary type.

#### A Case for Diagnosis Nodular Lesions of the Face? Presented by Dr JACK WOLF

L C, a woman aged 38, is presented from the dermatologic clinic of Mount Sinai Hospital with two nodular lesions on the right side of the face of approximately two years' duration. The lesion over the right zygoma is an approximately pea-sized, elevated, papular, glistening lesion, pale pink and of a fleshy, elastic consistency. The base is not indurated. The lesion below is somewhat similar in appearance, but with less elevation and a rather flattened surface, as a result of attempted removal (excision for biopsy), and possibly of previous roentgen therapy, the lesion having received 700 r in divided doses. There is an approximately dime-sized induration of the tumor bed.

The patient received antisyphilitic treatment in irregular and rather haphazard fashion for six years or more. The Wassermann reaction of the blood has consistently been negative during the past few years. Oral administration of iodides did not influence the lesions.

Histologic examination was performed on three occasions, with the following reports:

1 "Fragment of skin showing granuloma with conspicuous eosinophilia."

2 "Section of skin showing striking capillary proliferation with a diffuse inflammatory reaction. The histologic picture is equivocal and could be that of granuloma or an inflamed angioendothelioma. I prefer the first alternative (granuloma) but would recommend that the patient be kept under close observation."

3 "Chronic nonsyphilitic inflammation with a conspicuous number of eosinophils and circumscribed necrosis. The histologic structure rules out sarcoid and tuberculosis, but the lesion could be a persistent papulous urticaria."

#### DISCUSSION

DR MAX SCHEER It has been impossible to make a clinical diagnosis, though it might be sarcoid, several histologic reports, however, do not bear out such a diagnosis. There are many eosinophils in the slide, and I thought the lesion might be one of those rare eosinophilic granulomas, but Dr Otani, of the department of pathology, saw the slide again and could not make a diagnosis. It is impossible to make either a clinical or a histologic diagnosis at present.

DR CHARLES WOLF I should like to ask the presenter whether at any time there was a discharge from the lesions. [Answer: No.] I was thinking of the possibility of actinomycosis.

DR CHARLES S MILLER I suggest the possibility of Spiegler-Fendt sarcoid. I had a patient with similar lesions, and examination revealed the pathologic changes of this sarcoid.

DR SAMUEL M PECK Surely the histologic picture gives some indication of the diagnosis. The very fact that three sections were taken and that these three

sections showed such diverse histologic structures proves that the lesion is not a specific granuloma. The histologic data, even if not specific, can be used to rule out certain conditions. In looking at the lesions, one would certainly think first of sarcoid. I cannot think of any type of sarcoid, either the Boeck or the Spiegler-Fendt, that would resemble the histologic pictures seen here. If one palpates the lesions, one feels a little cord connecting them. Why cannot the diagnosis be something simple? In the lower lesion, at the periphery one finds a few large follicular openings, resembling comedos. Why may this not be a chronic infection, cystlike lesion? When the sac is ruptured and the sebaceous material comes into contact with collagen, it forms a granuloma of a tubercloid type. I suggest the diagnosis of a beginning keloid in an infected cyst.

### Syringoma Presented by DR MAX SCHIFFER

I K., a man aged 49, is presented from the dermatologic clinic of Mount Sinai Hospital with an extensive eruption of at least ten, and possibly twenty, years' duration. The eruption is widespread. Lesions are present on the trunk, chiefly along the anterior aspect, on the inner aspect of the upper extremities and to a lesser degree on the thighs and neck. The greatest profusion of lesions occurs along the lower part of the chest wall and along the forearms, and here they are also particularly developed. The individual lesion is approximately the size of a matchhead, smooth, discrete, fleshy and of a moderately intense red color. The less developed lesions are smaller and are more yellowish.

Biopsy was reported by Dr Paul Klemperer to show a structure consistent with a diagnosis of syringoma. In the corium there were many cysts lined with epithelial cells.

### DISCUSSION

DR EUGENE T. BERNSTEIN: This is a classic case of syringoma occurring over the chest and extending to the extremities. The eruption is composed of fawn colored to yellow globoid nodules ranging from the size of a pinhead to that of a split pea and larger and presenting a somewhat waxy appearance. The lesions are slightly elevated. The patient has no subjective symptoms, and the general health is unimpaired. Syringoma usually occurs in women, and the establishment of the clinical diagnosis is not particularly difficult. The lesion is regarded as a new growth derived from misplaced embryonic sweat ducts or sweat glands. Werdman expressed the belief that the condition is a true adenoma of the sweat glands. Homma and Escher raised the question of the origin of syringoma in the apocrine glands (*Genesis of Syringoma*, *ARCH. DERMAT. & SYPH.* 33:700 [April] 1936).

DR E. W. ABRAMOWITZ: Histologic examination is the final desideratum in the diagnosis. Clinically, syringoma is frequently associated with other types of lesions, such as multiple benign cystic epithelioma of the eyelids and involvement of the axillary region. Many years ago at the Vanderbilt Clinic, Dr John Remer presented a case of syringoma in which he obtained involution with fractional doses of roentgen rays. In my first case I had a similar result. Fourteen or sixteen fractional doses (75 r each), unfiltered, caused a remarkable involution.

DR EUGENE T. BERNSTEIN: A distinction should be drawn between syringoma and multiple benign cystic adenoma (Jarish). Multiple benign cystic adenoma begins at the age of puberty, is frequently hereditary and is seen in several members of the same family. The lesions are conspicuous in their occurrence about the face. The origin of these growths is in the basal layer of the epidermis or similar cells of the hair follicles, and not from the sweat glands, as is the case in syringoma.

DR OSCAR L. LEVIN: This case represents a disease which is usually more localized. The histologic structure is characteristic of syringoma, and clinically several disorders are suggested. Multiple benign cystic epithelioma tends to be more localized to the chest, face and neck. The lesions are firm and tend to show central depressions. The histologic structure is different from that of syringoma, revealing strands and masses of epithelium, with a tendency to formation of cysts.

containing horny material. There may be structures suggestive of hair follicles and sebaceous glands. Syringocystadenoma is usually yellower and softer, and the pathologic picture resembles that of multiple benign cystic epithelioma, revealing also structures suggestive of tubules and coiled glands. In the present case the lesions are soft, as is usually observed in cases of syringoma, and generalized, and the diagnosis of syringoma must be accepted because of the histologic picture. Roentgen irradiation will not be of benefit in the first two lesions mentioned, but may be of value in destroying the syringoma.

DR CHARLES S MILLER. The diagnosis in a case of this type is usually made histologically. The term "syringoma" should be applied to a nevoid condition arising from the duct part of the sweat duct system. "Syringocystadenoma" is frequently used interchangeably with "syringoma," although it denotes a histologic picture in which there are more elements of the sweat ducts, some of which show dilatation. The term "spiroadenoma" refers to a nevoid condition arising from the coil, or secreting, portion of the sweat gland system.

DR JACOB SKEER, Brooklyn. In 1936 I saw a similar case, that of a single white woman aged 22 (Syringocystadenoma, *ARCH DERMAT & SYPH* 40 268 [Aug] 1939), with an eruption of exceptionally wide and unusual distribution of twelve years' duration. The lesions were irregular, flattened papules situated on the neck, shoulders, axillas, chest, hips and thighs. The histologic report by the late Dr D L Satenstein was syringocystadenoma. The patient had tuberculosis and was in a sanatorium. She received two courses of roentgen therapy, in doses of 150 r each, at intervals of two weeks, for a total of six treatments, after which the lesions appeared flatter. New lesions continued to appear. Three years later the lesions were still present.

DR MAURICE J COSTELLO. I should like to suggest to the presenter that if roentgen therapy is used here only one side of the body be treated. Dr Fox had a patient with a similar, but less extensive, eruption to whom fractional doses of roentgen rays were administered, causing involution of lesions on one side of the body.

## METROPOLITAN DERMATOLOGICAL SOCIETY

Royal M. Montgomery, M D, *President*

James Lowry Miller, M D, *Secretary*

*New York, Oct 15, 1945*

**Rosacea** Presented by DR JOSEPH C. AMERSBACH

A P, aged 48, shows hypertrophy of the nose associated with redness, telangiectasia and papulopustules. He has received roentgen therapy, applications of solid carbon dioxide, sulfur pastes and lotions, and dilute hydrochloric acid, with only moderate improvement.

The patient is presented for suggestions as to therapy.

### DISCUSSION

DR LESLIE P. BARKER. This patient had definite rosacea of the tip of the nose. The cause is difficult to determine. I think the best result can be obtained with scarification, but it would require repeated treatments. Peeling doses of cold quartz-mercury vapor radiation, along with scarification, may also help.

DR MAURICE J. COSTELLO. I do not think that this patient has rosacea. I think the eruption is a dilatation of the blood vessels of the bulbous portion of the nose, secondary probably to trauma. I have seen this clinical picture follow infections of the nose, such as carbuncles and furuncles, and, especially, operations on the nose and sinuses. There is nothing, in my experience, that will help him, short of surgical diathermy, in which one runs the risk of scar formation.

DR THOMAS N GRAHAM I am inclined to agree with Dr Costello I have cases similar to this at the New York Eye and Ear Infirmary in which there has been a nasal operation This patient does not show the characteristic features of rosacea The disturbance is probably a circulatory deficiency, which will not respond to any form of therapy

DR JOSEPH C AMERSBACH I have had many cases of this type, and often I am in doubt as to whether they are true cases of rosacea

**Epidermodysplasia Verruciformis** Presented by DR ROYAL M MONTGOMERY

C R, a white woman aged 28, has had the present disease for twenty years She was first seen April 13, 1945

There are many flat, shiny-topped papules on the fingers and the dorsa of the hands Many are grouped on the fingers Some are flesh colored, others are red There are similar flat, verrucous lesions on the dorsum of the right foot and the ankle

Roentgen therapy and six intramuscular injections of bismuth subcitrate have failed to produce any improvement

The biopsy report on a lesion (Dr Charles F Sims) follows "The epidermis presents an irregular surface, covered in part with a mild, loosely laminated horny layer At two points in the section there is moderate acanthosis In these areas the granular layer is absent for the most part The rete presents numerous vacuolated cells, producing a basket-weave effect The corium reveals no noteworthy changes"

The diagnosis is epidermodysplasia verruciformis

#### DISCUSSION

DR MAURICE J COSTELLO I agree with the diagnosis of epidermodysplasia verruciformis, although the eruption is not so extensive as in some cases that I have observed I believe that these lesions can be successfully treated with the electric cautery (fractional method)

DR THOMAS N GRAHAM I agree with the diagnosis It has been proved by biopsy

DR JOSEPH C AMERSBACH I understand that no new lesions have appeared since the onset I should therefore suggest excision with the scalpel rather than treatment by desiccation

DR LESLIE P BARKER I agree with the diagnosis of epidermodysplasia verruciformis, and I think these lesions should be destroyed by electric desiccation, as they often develop into basal cell epitheliomas I had a case of extensive involvement a few years ago in which superficial basal cell epitheliomas developed in the lesions Many lesions resembled atrophic lichen planus, while others resembled the papular type of lichen planus

DR ROYAL M MONTGOMERY I believe all lesions should be destroyed If not destroyed, some will later show epitheliomatous changes The patient does not approve of having them destroyed She realizes it will cause scarring

**A Case for Diagnosis (Dermatitis Venenata? Erythroplasia?)** Presented by DR LESLIE P BARKER

E K., aged 43, was first seen eight months ago, at which time he gave a history of having had a slightly itchy, nonpainful eruption on the glans penis of two months' duration The lesion practically cleared twice but soon recurred He denied taking any drugs, and neither he nor his wife used contraceptives His general health was good He denied having had any venereal disease

Examination reveals a patchy, circumscribed lesion involving the larger part of the distal half of the glans penis and extending around the meatus The lesion is bright red and granular, and there is a serous discharge with crusting

Treatment has consisted in use of fractional doses of roentgen rays, with a total dose of 600 r, and soothing ointments, such as starch in cold cream and plain white petrolatum. The patient has abstained from all friction or irritation. The Wassermann reaction of the blood was negative.

The biopsy report follows: "Sections of the lesion stated to have been removed from the penis disclosed edematous stratified squamous epithelium, which had undergone hyperplasia. A detached scale of parakeratosis was present. Leukocytes had infiltrated both the epithelium and the underlying stroma. The latter was the site of a profound chronic inflammatory reaction, with many plasmacytes and a few eosinophils. There were no pathognomonic changes."

#### DISCUSSION

**DR MAURICE J COSTELLO** This lesion impressed me as one of erythroplasia, especially since it began on the glans penis, increased gradually and slowly and never receded. The lesion must have a fair amount of exudation because it is covered with a crust. I think the lesion is preepitheliomatous and should be destroyed adequately. I have destroyed several of them with electric desiccation, sometimes repeating the treatment a second or a third time before the lesion finally disappeared.

**DR THOMAS N GRAHAM** I agree with Dr Costello.

**DR ROYAL M MONTGOMERY** A few years ago Dr Lapowski showed several cases of this type at a meeting of the Section of Dermatology and Syphilology, the New York Academy of Medicine. He used a paste of resorcinol and an aluminum tube as protection and had remarkable results. Since fractional doses of roentgen rays and soothing ointments have been used without results, destruction is now in order.

**DR JOSEPH C AMERSBACH** I believe this is the type of case in which a proper diagnosis cannot be made by microscopic study alone.

**DR RICHARD J KEFFY** I think this case falls in with 50 or 60 cases described by Madden before the Section on Dermatology and Syphilology at the annual session of the American Medical Association at Atlantic City, N J, in 1933 (Generalized Angiomatosis, *J A M A* 102:442 [Feb 10] 1934). He had studied carefully for a period of four or five years cases like this in which the lesions were resistant to local therapy but did respond to roentgen radiation and radium. He felt that the latter was the proper method of treatment. I have seen only 2 or 3 patients with this disease, and all have responded properly to roentgen or radium therapy. I agree with the diagnosis of erythroplasia.

**DR LESLIE P BARKER** I think this is a case of erythroplasia, although during the first few weeks that I treated this patient the eruption reacted more like dermatitis venenata. It cleared almost completely with soothing applications and then reappeared suddenly after the patient had applied an irritating ointment.

I hesitated to destroy the area with electrodesiccation because it involved the meatus. I shall use superficial radium therapy and report later on the result.

#### **Erythema Perstans** Presented by **DR ROYAL M MONTGOMERY**

**J S**, a Cuban aged 39, has had the present eruption for four years. He was first seen at the New York Skin and Cancer Unit on July 31, 1945.

In the groins, axillae and about the upper portions of the thighs he has erythematous, semicircular patches which have slightly raised, nonvesicular borders. The centers of the patches are slightly pigmented and scaly. They tend to heal spontaneously, with a new patch appearing nearby. The patient has had a duodenal ulcer.

Examination for tinea gave negative results. The Wassermann and Kahn reactions of the blood were negative.

Ten thousand units of penicillin was given on Sept 18, 1945 for a streptococcal infection. This caused a slight flare-up of the eruption.

## DISCUSSION

DR THOMAS N GRAHAM I think this is a case of erythema annulare centrifugum, because the patient gives a history of the annular lesions starting with a single papule which spreads peripherally to form a circle of papules. The lesions also show a crater-like sloping of the inner borders. This feature was described by Darier. Erythema perstans usually presents only one or two lesions. Both diseases are probably related to erythema multiforme. Dr Throne and I treated 5 patients with a bismuth preparation, 2 of whom apparently responded, but they had remissions (Graham, T N, and Throne, B. Erythema Annulare Centrifugum, *ARCH DERMAT & SYPH* 22 777 [Nov] 1930). We were therefore not certain whether or not bismuth therapy was effective.

DR RICHARD J KELLY I agree with Dr Graham. I think this case fits in with his description.

DR MAURICE J COSTELLO I agree with everything Dr Graham has said. I have heard that intramuscular injections of bismuth subsalicylate are of value in this dermatosis. I never had the success that others claim with this form of therapy. I should like to hear discussion on that point.

DR ROYAL M MONTGOMERY The term erythema perstans covers a wide variety of lesions. My impression of erythema annulare centrifugum is that concentric, multichromatic, halo-like lesions are present. In this case one sees one lesion only with a semicircular border. It was suggested by an internist, who saw this patient with me, that saline catharsis, together with succinylsulfathiazole, be prescribed. The patient has received this therapy for a week. He has shown improvement. The same therapy will be continued. He was taking 2 Gm of the drug every three hours with an alkali. If this does not help, a bismuth preparation will be given. (A week later the patient showed 80 per cent improvement.)

### Purpura Annularis Telangiectodes Presented by DR ROYAL M MONTGOMERY

J T, a nurse aged 18, has had the present eruption for one month. For the past year and a half there has been a small eczematous patch on the dorsum of the left foot. The newer lesions spread from this patch about one month ago.

At present there is a small dry, eczematous patch on the dorsum of the left foot. Small red papules are present in this area. There are many scattered pinpoint, red or telangiectatic papules near this eczematous area. These are also found on the dorsa of the toes of both feet and about the heels.

Examination of the blood showed 97 per cent hemoglobin (14.1 Gm per hundred cubic centimeters), 4,500,000 erythrocytes and 130,000 platelets.

The patient has been taking 300 mg of ascorbic acid daily. There has been no improvement.

## DISCUSSION

DR JOSEPH C AMERSBACH I agree with the diagnosis, and I myself have had several cases of this type in the past few years. It is my belief that a further search should be made for foci of infection. However, many times no foci of infection can be found. When no such foci are present, I am generally content to use roentgen rays and lotions, which usually control the associated pruritus and clear up the eruption temporarily.

DR RICHARD J KELLY I think this patient has a vasomotor disturbance. I believe a test of vascular function should be made before any other determinations. She should have a thorough examination, including hepatic function tests. If there is any way of testing her for sensitivity to histamine or histaminase, it should be done.

DR MAURICE J COSTELLO I do not think any one can make that diagnosis clinically. It may be suspected. I presented patients before several of the societies whom I had observed for years. One was a young woman with an eruption which resembled this in the beginning and later showed areas of atrophy, hyperpigmentation and depigmentation. That girl went from one dermatologist to another and

from clinic to clinic. I finally gave her gold sodium thiosulfate. After she had received twelve injections the eruption disappeared. Examination three years later showed that she had had no recurrence except for a little breaking down around the ankle, which had occurred only a few days previously.

DR THOMAS N GRAHAM: The lesion on the left ankle could well be hypostatic eczema. The other lesions are purpuric and could be on a hypostatic basis. The patient stands a great deal, resulting in dilatation of the veins. I cannot see anything at present on which one could base a diagnosis of purpura annularis telangiectodes. There is no atrophy, as Dr Costello pointed out, and no annular arcus. I favor a diagnosis of hypostasis, producing eczema and purpura.

DR J LOWRY MILLER: I agree with the statements of the last speaker. I have successfully used blistering doses of ultraviolet radiation in 2 cases. There is no danger in this therapy, and it may be successful.

DR ROYAL M MONTGOMERY: As for giving blistering doses of ultraviolet radiation therapeutically, it would be best to check on the condition of her vascular system first. I do not believe this therapy would help. This case suggests an early purpura annularis telangiectodes. Perhaps I should have presented the case with the present diagnosis and a question mark.

### **Dermatophytosis of the Hands and Feet Tinea Corporis (Glabrosa)**

Presented by DR ROYAL M MONTGOMERY

J G, a white man aged 24, who was first seen on Oct 5 1945, has had the present eruption for two years and three months. He was with the Navy in the Solomon Islands when the eruption first started.

On the dorsum of the right hand there is a dull red, scaly dermatitis with some formation of papules. On the index and ring fingers of this hand there is a white linear streak across the center of the nail plates. This eruption extends on to the wrist. On the palm the skin is thickened, dull red and slightly scaly. Several dried pustules are present. These also extend on to the wrist. The left hand is normal.

There is a red, scaly patch on the outer side of the right ankle just behind the malleolus. On the dorsa of both feet there are scaling, erythematous patches with some extension toward the toes. On the soles and extending on to the instep there are scales and erythematous macules. On the anterior surface of the right knee there is also a scaly, red patch. There are similar areas in the groins and on the buttocks.

Examination of material from the dorsum of the hand and the foot for tinea gave positive results. Cultures have not had time to grow.

### **DISCUSSION**

DR R C CARLISLE (by invitation): I have seen many cases similar to this. It is often necessary to try many kinds of therapy until a suitable one is hit on. Recently, I saw a case of the infection contracted in Guadalcanal which had not responded very well to any type of treatment. The lesions are often made worse with ultraviolet radiation therapy, in fact, it is easy to make them worse.

DR RICHARD J KELLY: Dr Montgomery knows more about how to kill the fungus than I do, on the other hand, I am inclined to agree with Dr Carlisle that trial and error is usually necessary. I would suggest that the parts be elevated and kept dry until more drastic measures are decided on. I should use roentgen radiation and powder at the present time. Climatic conditions were responsible for the severity of the lesions in many instances. Even the natives had similar conditions.

DR MAURICE J COSTELLO: It is my opinion that the patient has an infection with *Trichophyton purpureum*. No one sees many cases of this disease in private practice, as is well known, the infection is resistant to therapy. I have had a degree of success with anthralin ointment (1 or 2 per cent anthralin in a petrolatum base) and chrysarobin, 10 to 20 per cent.

DR THOMAS N GRAHAM I agree with the diagnosis Vioform, 10 to 20 per cent in petrolatum, might also be tried This ointment is effective in some cases of dermatophytosis in which other measures produce no improvement

DR J LOWRY MILLER I have used both undecylenic acid and propionic acid in these cases, without any benefit

DR ROYAL M MONTGOMERY I agree that these cases always present a problem Roentgen irradiation is contraindicated because it results in no therapeutic response I think the lesions should be treated with strong fungicidal remedies This will be a good case in which to try it This patient presents another problem in that he is training to be a chiropodist If he does not clear his hand, he may infect his patients, and incidentally increase his business tremendously He was told by five Navy dermatologists that his present disease is incurable Perhaps I should agree with them

#### A Case for Diagnosis (Vascularitis of Unknown Origin?) Presented by DR J LOWRY MILLER

R S, a woman aged 21, was seen by the presenter at the Presbyterian Hospital on Sept 8, 1945 At that time she complained of a macular rash on the forearms and the dorsal and palmar surfaces of the hands of six months' duration During the six months the rash had been present a splenectomy was performed for idiopathic thrombopenic purpura The symptoms prior to operation had been bleeding gums, ecchymoses of the body, epistaxis and tarry stools The platelet count prior to operation had fallen to 4,000, and by the tenth postoperative day it was 351,000 The patient had postoperative elevations of temperature to as high as 104 F, for which penicillin, sulfadiazine and blood transfusions were given Penicillin and sulfadiazine had no effect on the temperature, which gradually cleared as a pleural effusion on the left side absorbed The patient did not complain of symptoms connected with the rash but did have generalized weakness A diagnosis of Still's disease (multiple rheumatoid arthritis) had been made on his admission to Presbyterian Hospital in 1938 Similar cutaneous lesions were described as present at that time

On both surfaces of the hands and, to a less extent, on both surfaces of the forearms, there are red, split-pea-sized macules which fade on pressure There is no scaling

The electrocardiogram was normal A blood count showed 11 Gm of hemoglobin per hundred cubic centimeters, 4,000,000 red blood cells and 10,000 white blood cells, with a normal differential count The sedimentation rate varied from 90 mm in one hour to normal The blood platelet count at the time of her discharge from the hospital was 351,000 Roentgenologic examination of the chest revealed nothing abnormal The urine was normal except for a 2 plus reaction for albumin

#### DISCUSSION

DR RICHARD J KELLY This patient has a muscular dystrophy I think that she also has a disturbance of the sympathetic nervous system Her palms and feet perspire constantly She has lost 20 pounds (9.1 Kg) in weight Her appetite is normal to all appearances, but she does not gain any weight I agree with Dr Miller when he says that the lesions on the shoulders might be evanescent They have appeared and have gone away before I think the diagnosis is some type of progressive muscular dystrophy, which I shall have to leave for the other members to decide on

DR MAURICE J COSTELLO I agree with the diagnosis of Still's disease This girl has bilateral synarthrosis with large joints, which show no changes on roentgenographic examination, in addition to anorexia, loss of weight, a cachectic appearance and retardation of growth of the skeletal system I believe that the eruption she presents is associated with the disease The prognosis is unfavorable

DR THOMAS N GRAHAM I do not think that this case is one of dermatomyositis with acute lupus erythematosus The lesions on the dorsa of the hands

are not the type found in lupus erythematosus. I cannot suggest a diagnosis in this case.

DR JOSEPH C. AMERSBACH: I am not acquainted with the diagnosis in this type of case. Since the lesions fade, I believe the eruption to be a toxic manifestation associated with the general condition of the patient.

DR J. LOWRY MILLER: I presented this case for suggestions as to the significance of the macular lesions. On the one hand, they may represent the early stages of one of the so-called vascular diseases, on the other hand, they may be the residua of gradually resolving Still's disease. The fact that they were described when the patient had Still's disease, at the time she was first observed, is in favor of the latter view.

#### Granuloma Annulare Presented by DR J. LOWRY MILLER

C. H., a girl aged 7 years, was seen at the Vanderbilt Clinic with the complaint of red lesions on the right thigh and right ankle, which had been present for one year. The patient had noted no symptoms except the gradual enlargement of the lesions. She denied having taken any medicament by mouth.

On each of the aforementioned locations there is present a circular lesion the size of a silver dollar. The border is made up of erythematous, closely grouped nodules, and the center is clear. In places the ring is undergoing involution and has a crescentic configuration.

#### DISCUSSION

DR ROYAL M. MONTGOMERY: I agree with the diagnosis. The border is less erythematous but more indurated than that in the case I presented. The 2 cases belong in the same category.

DR JOSEPH C. AMERSBACH: I agree with the diagnosis of granuloma annulare.

DR LESLIE P. BARKER: The lesion consists of split-pea-sized, firm, grayish nodules arranged in a circinate fashion. Clinically it is typical of granuloma annulare.

DR RICHARD J. KELLY: I agree with the diagnosis. May I ask the presenter whether roentgenograms were taken of the chest, the fingers and the extremities?

DR J. LOWRY MILLER: No, they have not been taken yet.

DR MAURICE J. COSTELLO: I think I agree with the diagnosis of the lesion on the ankle. I was under the impression that in granuloma annulare the border is continuous. In both lesions the border is absent in one segment, which made me feel that the child has erythema annulare centrifugum. A biopsy should be performed to clarify the point.

DR J. LOWRY MILLER: At the time the patient was first seen erythema annulare centrifugum was considered as a possible diagnosis. I believe this is a case of granuloma annulare because the lesion is present in a child and because of the hard border. I have seen, and I think there have been described, cases in which part of the border has disappeared.

NOTE.—Histologic examination was reported to reveal granuloma annulare.

#### A Case for Diagnosis (Psoriasis? Onychomycosis?) Presented by DR J. LOWRY MILLER

R. B., a woman aged 49, was first seen by the presenter one week ago, complaining of a yellowish discoloration and crumbling of the nail of the fourth finger of the left hand. She had noticed this change for the past three months. She had never had any cutaneous lesions or symptoms of arthritis.

The entire nail of the left fourth finger is yellowish, thickened and distorted. The bases of all the other finger nails are covered with stippling. There are no changes along the edges of the nails. Between the third, fourth and fifth toes there is whitish maceration. The toe nails are normal. The scalp and elbows are clear.

Fungus was revealed on microscopic examination of material from the toes but not from the finger nails

## DISCUSSION

DR JOSEPH C AMERSBACH I suggest that the diagnosis be withheld until a report of the culture is obtained

DR LESLIE P BARKER I think the condition of the nails is due to a fungous infection rather than to psoriasis There are no lesions elsewhere on the body, and the nail shows ridging, discoloration and thickening, with only pseudopitting The pitting of psoriasis is usually characteristic, although not present in all cases Cultures should be made for fungi

DR R C CARLISLE (by invitation) I favor the diagnosis of fungous infection

DR RICHARD J KELLY I agree with Dr Carlisle that it is a fungous infection

DR MAURICE J COSTELLO The evidence is in favor of psoriasis, for fungous infection to involve all the finger nails takes years, then, again, usually one or two nails would be free of infection All the nails are involved in this case I think the pitting is suggestive of psoriasis

DR THOMAS N GRAHAM I agree with Dr Costello There does not seem to be any undermining of the margin of the nail, which one usually sees with fungous infections of the nails I thought I saw definite pitting, which of course is a feature of psoriasis of the nails

DR ROYAL M MONTGOMERY One always hesitates to make a diagnosis of psoriasis of the nails without other cutaneous lesions Dr Costello mentioned that pitting developed in all the nails at the same time This is against the diagnosis of onychomycosis Clinically it does not impress me as a fungous infection Several examinations for tinea should be done to rule out that possibility

DR J LOWRY MILLER Even if fungi are found in culture of material from the nails in this case, I doubt whether fungous infection is the underlying cause The pitting of all the nails, the absence of paronychia and the sudden onset all favor a diagnosis of psoriasis However, that diagnosis cannot be made until more positive proof is present

#### A Case for Diagnosis (Superficial Epithelioma? Bowen's Disease? Roentgen Ray Dermatitis? Neurodermatitis?) Presented by DR J LOWRY MILLER

A I, a woman aged 62, was first seen at the Vanderbilt Clinic Oct 8, 1945, complaining of lesions on the left side of the chest, the left axilla, the right shoulder and the extensor surfaces of both elbows She stated that the lesion on the left side of the chest had been present for five years, the lesion in the left axilla for three months, the lesion on the right shoulder for many years and the lesions on the elbows for several years

She had had a mastectomy of the left breast for cancer twenty-seven years ago and a similar operation for cancer of the right breast thirteen years ago Metastasis to the nodes of the right axilla had occurred before the second mastectomy, and she was given massive radiation therapy for these nodes For the past five years she had noticed a gradually enlarging lesion of the left side of the chest, and for the past three months, a similar lesion in the left axilla Itching lesions have been present on both elbows for several years

On the left side of the chest there is an erythematous lesion the size of a 50 cent piece studded with pinhead-sized, hyperkeratotic areas In the left axilla there is a dime-sized, slightly elevated circular lesion with no ulceration On the left side of the chest, the right axilla and the right shoulder there are white atrophic areas in which there are many telangiectases On the elbows there are red, lichenified patches

## DISCUSSION

DR LESLIE P BARKER The lesions have the appearance either of Bowen's disease or of superficial basal cell epithelioma developing on a dermatitis due to roentgen rays They should be destroyed by electrodesiccation

DR R C CARLISLE (by invitation) The largest lesion looked like a superficial basal cell epithelioma It could be a lesion of Bowen's disease

DR RICHARD J KELLY I think the lesion might be classified as Bowen's disease clinically, but biopsy should be performed There are nodules under her skin I remember a case Dr Amersbach presented before this society two or three years ago in which there was multiple basal cell epithelioma I should be interested in having him discuss this case I found other nodules that might or might not be described as pathognomonic

DR MAURICE J COSTELLO It is impossible to make a definite diagnosis of epithelioma at this time, but I should suspect the presence of such a neoplasm, since one of these lesions occurred on devitalized skin I think it should be treated as prickle cell epithelioma

DR THOMAS N GRAHAM My impression is that the eruption in the left axilla may be seborrheic dermatitis The patient has seborrhea of the scalp A biopsy of the other lesions should be made before deciding on the treatment They may well be epitheliomas

DR ROYAL M MONTGOMERY Without a biopsy, I favor the diagnosis of superficial basal cell epithelioma rather than Bowen's disease In the cases of Bowen's disease I have seen there was not as much infiltration as in cases of superficial basal cell epithelioma In the former disease there is a smoother lesion However, I think a biopsy must be made to make the exact diagnosis

DR JOSEPH C AMERSBACH The lesion impressed me as one of Bowen's disease, if not this, it may be either basal or prickle cell epithelioma Regardless of the true diagnosis, I think that the adequate treatment is electrosurgical The lesion in the axilla is probably associated with other areas of dermatitis on the arms and elbows

DR J LOWRY MILLER This case is one of unusual interest because of the history of cancer of one breast twenty-seven years ago and cancer of the other breast thirteen years ago The diagnosis in both instances was established by biopsy In the second instance metastasis to the regional axillary node had occurred The treatment was radical mastectomy followed by roentgen irradiation A superficial type of epithelioma arising in an area of dermatitis due to roentgen irradiation presents to my mind a difficulty in classification

### **Erythema Multiforme Bullosum and Dermatitis Medicamentosa [Sulfonamide Compounds]** Presented by DR MAURICE J COSTELLO

K R, a Negro aged 52, has an eruption which has occurred in three more or less separate attacks over the last two months At present the third exacerbation is subsiding The patient began to have vesicles on the tongue about two months before admission (Aug 1, 1945) Two or three days previously he had had a sore throat and mild nasopharyngitis, which he believes was a "cold" He was treated (for the lesions on the tongue) by a local physician, who gave him tablets and a mouth wash In about three weeks the lesions cleared up Two weeks after the first lesions had subsided, the lesions on the tongue reappeared, and at the same time a small, tack-head-sized vesicle appeared on the dorsum of the left wrist This blister ruptured, and the subsequent denuded area spread peripherally to become the size of a nickel The denudation remained fairly superficial, and subjective symptoms were slight He visited another local physician, and, after local and oral therapy for about a week, the lesions again regressed Two weeks later vesicles reappeared on the tongue and in the mouth, the lesion on the wrist flared up again and was the site of a papulovesicular eruption New vesicular lesions appeared on the arms, scrotum, penis and legs and, lastly, on the face and forehead

These new lesions became denuded and especially raw on the scrotum, where pruritus was severest

Two months before the initial outbreak he had had sexual intercourse, but not since. He has had several colds during the winter and one a short time before the initial outbreak of the present eruption. The temperature has been normal. Urinalysis and examination of the blood gave normal results. On Oct 3, 1945 the Wassermann and Kahn reactions of the blood were negative. Dark field examination for *Treponema pallidum* on Oct 2, 1945 gave negative results.

#### DISCUSSION

DR THOMAS N GRAHAM I agree that the most likely diagnosis is erythema multiforme bullosum, probably due to medication with sulfonamide compounds. Bullous eruptions are not uncommon after ingestion of these drugs.

DR ROYAL M MONTGOMERY An interesting fact about cases of sulfonamide dermatitis is that a flare-up may occur when one thinks the patient is well on the road to recovery.

DR LESLIE P BARKER The eruption was typical of erythema multiforme bullosum. The interesting feature, however, was the appearance of the eruption so long after use of the drug had been stopped. It is common for sulfonamide eruptions to appear from nine to fourteen days after the drug is discontinued, but in this instance it was considerably longer.

DR J LOWRY MILLER I have seen a similar case in which there was this relatively long period after taking the drug before the onset of symptoms.

DR R C CARLISLE (by invitation) The picture in this case is compatible with the present conception of drug sensitization. A period of incubation is required before the patient is sufficiently sensitized to whatever residual amount of the drug remains in the body. Also, this sensitization, once occurring, does not necessarily remain but may disappear and reappear, thus giving rise to recurring eruptions without further ingestion of the offending drug.

DR MAURICE J COSTELLO In my experience, bullous eruptions following sulfonamide drugs are not frequent. The interesting feature in this case is the loss of so much fluid and blood from the mucous membrane.

#### Erythema Multiforme Bullosum (Due to Sulfonamide Medication).

Presented by DR MAURICE J COSTELLO

J W, two weeks previous to admission, was treated by a local physician with sulfathiazole for "lung trouble." He took the drug for fourteen days (dosage unknown). Two days before admission (October 1) his lips became swollen, edematous and denuded and began to bleed. A day later there were a slight bloody discharge from the penis and vesicles "all over the body."

On his admission, examination showed edematous, bleeding lips and buccal mucous membranes and a generalized eruption of flaccid, irregular bullae. The patient had had a sore throat one week before the outbreak of the present eruption.

The Wassermann reaction of the blood was negative, the blood count and the urine were normal. The temperature was normal. The patient felt quite ill when admitted and for two to three days afterward, but at present has few general complaints.

#### DISCUSSION

DR LESLIE P BARKER The lesions have the appearance of a fixed eruption. I should investigate the possibility of the patient's having taken any phenolphthalein, either as a cathartic or in foods or candies, it is often used as a coloring in confectionery.

DR THOMAS N GRAHAM I agree with the diagnosis of erythema multiforme bullosum. I do not think the eruption was apparent enough tonight to justify that diagnosis, but from the description I should accept it.

DR ROYAL M MONTGOMERY This case impresses me as one of an eruption caused by a drug. The lesion on his arm makes one strongly suspicious of phenolphthalein because of the color. He may have ingested it in candy or cake. Phenolphthalein may cause a vesicular or an eczematous eruption.

DR MAURICE J COSTELLO I agree with the diagnosis that this is a fixed eruption, probably due to a drug. He had an exacerbation of previous lesions after ingestion of the drug, such as the formation of an erythematous halo, the center of the lesions becoming bullous.

### PHILADELPHIA DERMATOLOGICAL SOCIETY

Donald M Pillsbury, M D, *Chairman*

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Oct 19, 1945

#### Granuloma Annulare Presented by DR MEYER L NIEDELMAN

M D, a white man aged 50, of good general appearance, three years ago noted a lesion on the inner proximal area of the right index finger. It was treated with roentgen rays and now appears as a circumscribed area of erythema with atrophy in the center. There is a suggestion of roentgen ray dermatitis. The present lesion began nine months ago and is situated on the inner dorsal surface of the right hand. It is annular and measures 3.5 cm in diameter. The central area is free, and the surrounding border is elevated and infiltrated, the border is studded with fine, discrete, pinkish papules. There is a similar, smaller lesion on the left index finger. There are no subjective symptoms.

The patient has had diabetes for six years. The blood sugar level on October 1 was 186 mg per hundred cubic centimeters. The urine was normal.

The patient has received four treatments with roentgen rays, totaling 300 r, and two intravenous injections of gold sodium thiosulfate, 10 mg per dose. The lesions show about 50 per cent improvement.

#### DISCUSSION

DR V PARDO-CASTELLO, Habana, Cuba (by invitation) All of us noticed the deep infiltration and the somewhat yellowish color of this infiltrate when the skin was devoid of the superficial erythema, that is, when the blood was forced out of the capillaries by pressure on the skin. Because the patient has a high blood sugar level, I thought of the possibility of necrobiosis lipoidica diabetorum. Of course, without a biopsy the diagnosis is tentative.

DR MEYER L NIEDELMAN When the patient was first seen, the lesion seemed typical of granuloma annulare. It is a bit altered now, owing to the roentgen therapy. There is no destruction of tissue, such as is seen in necrobiosis lipoidica diabetorum.

DR MORRIS MARKOWITZ On the index finger of the right hand there is a bizarre, apparently bullous eruption. Could this be a new disease, granuloma annulare bullosum?

#### Dermatitis Herpetiformis Presented by DR CARROLL S WRIGHT and DR MEYER L NIEDELMAN

W A, a white man aged 50, of good general appearance, presents scattered over the chest, gluteal areas and legs grouped excoriations, which are ruptured vesicles. There are lesions on the scalp, scrotum and penis. There is none in the mouth.

#### DISCUSSION

DR CARROLL S WRIGHT This case is presented, not as unusual but as a fairly typical example, I believe, of this disease for the purpose of instigating a

discussion of its therapy. For many years it was thought that one drug had a more or less specific action on this dermatosis, i. e., solution of potassium arsenite U. S. P., or some other preparation of arsenic. Recently, fairly good temporary results have been obtained with sulfapyridine. Failures also occur.

DR MEYER L. NIDELMAN. I recently had a patient with dermatitis herpetiformis (gestational type), which began about the seventh month of her pregnancy. She was given injections of about 3,000,000 units of penicillin, without any effect. The eruption persisted for five months after the baby was born and then disappeared.

DR DONALD M. PILLSBURY. My experience is confined to 1 case, but so far as my observation goes, penicillin therapy was a complete failure.

DR MARJORY K. HARDY. I have recently seen 2 cases in which penicillin was given, with no improvement.

DR J. M. SCHILDKRAUT, Trenton, N. J. Theoretically, penicillin is not indicated. Good results are obtainable with sulfapyridine.

DR DONALD M. PILLSBURY. I recall a discussion at the Royal Society of Medicine during which Barber emphasized that sulfapyridine is superior to the other available sulfonamide drugs in treatment of dermatitis herpetiformis. I think he also stated that he kept many of his patients on small doses of sulfapyridine for a long period.

DR HERMAN BEFRMAN. How was the diagnosis arrived at? Superficially, the eruption resembles the scratch dermatitis seen with pediculosis corporis.

DR E. R. GROSS. My colleagues and I had a patient whom we treated with 2,400,000 units of penicillin, without any effect. We have also seen patients with dermatitis herpetiformis treated successfully with one sulfonamide drug but intolerant to another. After treatment is changed to the use of sulfapyridine, they get along well. I believe that there is a neurogenic element in dermatitis herpetiformis. This patient had an exacerbation following a neurogenic upset.

DR ISADORE ZUGERMAN. Virus infection should be considered a cause of dermatitis herpetiformis.

DR DONALD M. PILLSBURY. Evidence has been brought on that point by Urbach. I do not believe it has ever been confirmed entirely, and further study is needed.

#### Cushing's Adrenogenital Syndrome. Presented by DR MEYER L. NIDELMAN

M. H., an unmarried Negro woman aged 20, presents generalized hirsutism, more evident on the masculine bearded areas, which necessitates shaving daily. The patient has previously been more obese than at present and has a broad face, thick neck and heavy shoulders. The hips are broad. She has a male escutcheon. The clitoris measures about 1 inch (2.5 cm.) in length, and the vulva is atrophied. The patient's grandmother had hirsutism of the chin. The patient had the usual diseases of childhood. She first noticed a growth of hair on the chin, face and pubic region at the age of 7 years. This gradually became generalized as she grew older. She was overweight from the age of 7 to 19 years. Menstruation began at the age of 17 and has been irregular or delayed, recurring at three month intervals. The flow is scanty. There is no dysmenorrhea. She also has severe headaches.

The blood pressure is 114 systolic and 60 diastolic. The heart and lungs are normal. The visual fields and eyegrounds are normal. Pelvic examination reveals no abnormalities. The breasts are normal. Libido is normal.

Chemical studies of the blood, urinalysis and a complete blood count gave normal results. Serologic examination of the blood for syphilis gave negative results. A roentgenogram of the sella turcica revealed nothing abnormal. Perirenal roentgenographic studies after injection of air showed a normal condition. The patient was operated on in August 1945, and both adrenal glands were observed to be small and atrophic. Biopsy of a specimen of one adrenal gland revealed atrophy and sclerosis of the cortex. The ovaries and tubes were normal.

## DISCUSSION

DR MEYFR L NIEDELMAN In a recent report of 33 cases of hirsutism, there were 4 cases of atrophy of the adrenal glands. This abnormality was designated as Cushing's adrenogenital syndrome. This case fits perfectly into that group. Therapy has been valueless in such cases.

DR J M SCHILDKRAUT, Trenton, N J Schamberg used to cite the case of a woman who had ovaries and testes, and when her ovaries were removed the hirsutism cleared up.

DR FRED D WEIDMAN Perhaps the explanation of that is that when destruction of the adrenal tissues has proceeded sufficiently (without rapid destruction, as in tuberculosis) there is a compensatory hypertrophy of the normal chromaffin tissue elsewhere in the body, such as that in front of the vertebrae. Normally there are little cords of chromaffin tissue there, even extending as far upward as the line of the coronary vessels. That was determined many years ago in connection with cases of complete tuberculous destruction of the adrenal glands, and yet the patients did not have a deficiency of the adrenal glands.

**Larva Migrans** Presented by DR CARROLL S WRIGHT and DR E R GROSS

R J, a white boy aged 2 years, has typical lesions over the flexor and dorsal surfaces of both wrists. The eruption began one month ago. Two days previously he had been playing in a sandpile near his Florida home. The sandpile was frequented by dogs. The child is being treated with fuadin, 2 cc given intramuscularly every three days. He has had fifteen injections to date.

## DISCUSSION

DR E R GROSS Treatment with fuadin is not the therapy of our choice. The physician referred the patient to us for continuation of the fuadin therapy. The child has had fifteen injections, with no improvement. With a few lesions we used ethyl chloride, with pronounced improvement.

DR D M SIDLICK What advantage is there in treating this disease with fuadin rather than with ethyl chloride? My personal experience is limited, but two or three years ago I presented a case in which only two or three treatments with ethyl chloride were required to eradicate the disease. The woman had an extensive eruption, involving not only the hand but the forearm as well.

DR FRED D WEIDMAN In cases in which there are hundreds of lesions, like those that I saw in Jacksonville, Fla., it would be a long process to use ethyl chloride on every one of the lesions. Moreover, it is generally known that the first application does not catch the parasite. It might prove that in such cases fuadin would be preferable.

DR V PARDO-CASTELLO, Habana, Cuba (by invitation) In cases in which there may be hundreds of larvae the best treatment is solid carbon dioxide, not the kind used in offices and hospitals, but the industrial product, the kind that comes with ice cream in the form of a cake. It is applied on the surface every other day without pressure.

**Keratosis Palmaris et Plantaris (Epidermodysplasia Verruciformis?)**

Presented by DR PATRICIA DRANT

M P, a white woman aged 31, first noticed thickening of the skin on the palms and soles at the age of 8 years. Discrete, verrucous lesions appeared on the dorsa of the hands when the patient was 13 years of age. Five years ago numerous keratotic and verrucous lesions, associated with pigmentation, appeared on the neck and forehead, particularly about the hair line. Verrucous lesions appeared on the legs in August 1943, a month after confinement. These lesions began as "running sores." The patient's 2 children were presented with her. A son, born in April 1935, first had lesions on the palms and soles when he was 7½ or 8 years of age.

A daughter, born in May 1936, presented lesions simultaneously on the palms and soles at the same age

## DISCUSSION

DR MEYER L NIEDELMAN This case fits into the picture of epidermodysplasia verruciformis. It is rather typical. This patient will have to be watched for the development of epithelioma, which occurs in a certain proportion of cases of this disease. I think a biopsy will confirm the diagnosis of epidermodysplasia verruciformis.

DR DONALD M PILLSBURY I had the feeling that the possibility of Darier's disease (keratosis follicularis) should be considered in the mother.

DR MARJORY K HARDY Has any one seen the two diseases together?

DR MEYER L NIEDELMAN Epidermodysplasia verruciformis is a nevroid dyskeratosis, but not an avitaminosis. This condition does not respond to vitamin A therapy. Because of the configuration of the lesions on the body and the prominent keratoses of the palms and soles, I believe that the mother has Darier's disease (keratosis follicularis) in addition to epidermodysplasia verruciformis. The two diseases have been reported in the same patient.

## Lupus Erythematosus Presented by DR PATRICIA DRANT

W H M, a white woman aged 47, in February 1944 visited in Florida. She was physically and nervously exhausted. Her hair started to come out badly at this time. She states that she had always been subject to sun poisoning, even on moderate exposure to the sun, the reaction being characterized not only by erythema but by a pruritic, papular eruption. She had such a reaction, probably slightly severer than usual, during the two weeks she was in Florida. Two weeks after her return she broke out on both cheeks and the right ear with an erythematous eruption, apparently similar to the one now present on her left cheek. She sought treatment from a specialist immediately. She was first given one injection of a gold preparation, to which she had considerable reaction. This therapy was discontinued, and she was given a series of injections of a bismuth compound. Later she was given smaller doses of a gold preparation, to which she responded more favorably. She was discharged in February 1945. In July she had an acute recurrence.

A complete blood count on Sept 5, 1945 revealed 72 per cent hemoglobin, 4,250,000 erythrocytes, 4,000 leukocytes, 70 per cent segmented polymorphonuclear cells, 26 per cent lymphocytes and 4 per cent stab forms. The Kolmer and Kline reactions of the blood were negative.

Biopsy was reported on by Dr Fred D Weidman as follows: "The epidermis was atrophic, with absence of interpapillary pegs. The only abnormality in the corium consisted of hyperplasia of the cells in the sheaths of the hair follicles. These were strictly confined to the hair follicles, i. e., they did not infiltrate the surrounding parts. These cells were more closely crowded than normal, and the nucleus was of young and proliferative type. This has led to enlargement of the hair follicle and a certain amount of distortion of its form." In the summer of 1945 the patient was given quinine sulfate orally and local applications of iodine and a sun screen cream, without result.

## DISCUSSION

DR E R GROSS Dr Carroll Wright and I have observed this patient for over a year, and it is our opinion that the lesion belongs under the head of Darier-Roussy sarcoid. She responded favorably to therapy but has had remissions and exacerbations. When her general health improved, she gained weight. When she had a nervous upset, she lost considerable weight and the lesions reappeared. The patient was given injections of gold sodium thiosulfate and also of liver extract. We felt that the only way we could produce improvement in the eruption was to improve her general health.

DR PATRICIA DRANT There was a time—when I took the biopsy specimen which Dr Weidman studied—when I thought from its clinical aspect that the eruption might be granuloma annulare.

DR MORRIS MARKOWITZ Histologically the picture is not that of sarcoid or lupus erythematosus. The lesion has elevated borders not unlike erythema elevatum diutinum perstans. On palpation one senses an increase in local temperature. I think the lesion is a form of erythema elevatum diutinum perstans.

DR FRED D WEIDMAN I do not think it is that. I do not believe that the section explains all the infiltration one can detect by palpation of the ring. It is a deep infiltration, yet the only pathologic changes I could see in the section were those in the hair follicles. I shall cut through the rest of the paraffin block so as to catch anything there is in it. This case recalls one that Dr Corson presented many years ago at a meeting of the American Dermatological Association, concerning which there was no agreement on the diagnosis. In this case the ring was back of the ear. Three or four weeks later Dr Wise said to me "This is a case of porokeratosis, about which we have had so many discussions in the society." Gilchrist thought that the lesion was tuberculosis because there were giant cells in the infiltrating part. The center was atrophic, just as in the present case.

DR PATRICIA DRANT The skin looks normal to me. I do not think the center of the lesion is atrophic.

DR FRED D WEIDMAN It is a peripherally spreading process. I feel that one would see more if one got down into the subcutaneous fat.

DR E. R. GROSS The type of lesion is always the same.

DR FRED D WEIDMAN I do think it is lupus erythematosus.

DR DONALD M PILLSBURY This case is representative of a group of cases with sensitivity to sunlight in which the eruption appears like lupus erythematosus. It is difficult at times to classify such cases accurately.

DR FRED D WEIDMAN There is a group of spreading annular eruptions, including erythema chronicum migrans of Lipschutz and this wandering gyrate eruption. Erythema figuratum perstans of Wende is another. I think that the eruption in the present case is chronic erythema multiforme.

#### **Lichen Planus (Lichen Ruber Moniliformis?)** Presented by DR JOHN W LENTZ

P. T., a white girl aged 19 years, presents a papular dermatosis tending to linear configuration, especially on the forearms, and limited to the arms and legs. It has been present for two years. The lesions have remained unchanged with treatment. The patient has received injections of bismuth subsalicylate intramuscularly.

#### DISCUSSION

DR FRED D WEIDMAN I think the sections exclude lichen planus. The appearance is more that of lichen nitidus.

DR ISADORE ZUGERMAN I suggest that a roentgenogram of the chest be taken and the blood sedimentation rate determined. I have in mind the possible diagnosis of lichen scrofulosus.

DR FRED D WEIDMAN The sections exclude that.

DR JOHN W LENTZ As I was not sure what it was, I presented this case with a questionable diagnosis of lichen planus or lichen ruber moniliformis. I wonder whether Dr Weidman has seen any section of lichen ruber moniliformis.

DR FRED D WEIDMAN I remember that the lesions in the cases of Wise were not violaceous, they were white. In lichen planus there is a definite hyperplasia of cells in the epidermis, and, of course, the interpapillary pegs give a saw-toothed effect. There is a zone of lymphocytes in this area. In the present case there is, to be sure, the zone of lymphocytes, but the processes in the epidermis are not hyperplastic. If anything, they are atrophic.

DR LOUIS GOLDSTEIN The lesions lack the color of lichen planus and are too large for lichen ruber moniliformis. I noticed the presence of the Koebner phenomenon in the place where the biopsy was performed.

**Pustular Syphilis** Presented by DR JOHN W LENTZ and DR MEYER L NIEDELMAN

M S, a white woman aged 41, was first seen on Sept 26, 1945. She had been bitten on the lower lip by her boy friend about three months previously. The latter had no apparent lesions on the skin or in the mouth. The lesion appeared first as a simple fissure, but later became elevated, forming a hard mass, with no pain. Submaxillary adenopathy then developed. About six weeks after the first appearance of this lesion, multiple lesions developed, beginning on the face and extending to the neck and trunk. On admission the patient had rather extensive pediculosis capitis, and the ova are still present. Distributed over the face, neck and trunk are numerous papules, nodules and pustules. Many of the pustules have large, brownish crusts. Many of these lesions are on an erythematous base. None is painful. In the midline of the lower lip there is a crust that is the remains of the previous chancre.

On October 3, the Kolmer reaction of the blood for syphilis was 4 plus and the Kahn reaction 2 plus. The urine was reported as normal. A complete blood count gave values within normal limits.

The patient received 50,000 units of penicillin every three hours for a total of 2,500,000 units. The eruption is decidedly improved.

DISCUSSION

DR D M SIDLICK: I could not see any frank pustular lesions. Some of the lesions on the body are rupial in character, and on the face they are large, flat nodules rather than pustules. One lesion on the neck presents all the characteristics of a granuloma. I think the eruption is a lesion of precocious tertiary syphilis.

DR MEYER L NIEDELMAN: The lesion on the lip was a typical chancre. At the time we saw the lesions they were definitely pustular, but it must be remembered that the patient has had 2,500,000 units of penicillin and that the lesions, of course, have undergone involution and what one sees now is of a rupial character.

DR JOHN F WILSON: It has been noted that the serologic reactions were not strongly positive. I wonder whether Dr Niedelman could explain that.

DR HERMAN BEERMAN: When arsenicals were used more extensively, a patient of this type would have been termed treatment resistant, and the low titer of the serologic reaction would be entirely in keeping with this. I think that even today she should be watched for the possibility of resistance to treatment.

DR SIMON KATZ: It occurs to me that a 2 plus reaction could be a zone phenomenon. Occasionally in cases of early syphilis one gets a positive complement fixation and a negative or doubtful flocculation reaction, until one carries out a titer determination and finds that the reaction is positive in high titers and doubtful or negative in low titers. It would be interesting to see what this patient's flocculation reaction is.

DR FRED D WEIDMAN: There is a patch of follicular keratosis over the chest. Might this be Darier's disease (keratosis follicularis)?

DR MEYER L NIEDELMAN: The patient said that she has had that patch for many years.

DR HERMAN BEERMAN: Are the lesions areas of seborrheic keratosis?

DR FRED D WEIDMAN: I do not think so. These are perifollicular.

**Trichotillomania** Presented by DR H H PERLMAN

R L, a white girl aged 7 years, when 2 years of age acquired the habit of playing with the hair of her scalp and twisting the hair with her fingers. At that time she did not pull her hair. The child persisted in this habit until the age of 5 years and practiced it continually in spite of reprimand, scolding and spanking. Later, hair pulling occurred at any time during the day. The child is a good

sleeper, her appetite is good, and she is not constipated. She does not receive medication of any kind and has experienced no nervous tantrums. There is no vomiting or other suggestion of nervousness. There is no evidence of masturbation.

The child was born after normal delivery at full term, she was breast fed for one month and then bottle fed. She had her first tooth at 8 months, walked at 10 months and talked at 14 months of age. She has had several attacks of bronchitis, she had chickenpox and measles at 2½ years, rubella at 6 years and whooping cough at 3½ years. She received diphtheria toxoid in infancy. A Schick test was performed months later, with a negative report. She was vaccinated during infancy and had immunizations against scarlet fever and whooping cough (Sauer vaccine).

She has received cod liver oil and vitamin C in the form of orange juice since infancy. No intestinal parasites have been noted in the stools. Her present height is 48½ inches (123 cm) and her weight 46½ pounds (21 Kg). This is 9 pounds (4.1 Kg) underweight. Physical examination showed nothing abnormal except for malnutrition and partial alopecia in the occipital and parietal areas of the scalp.

The urine was normal. A complete blood count revealed 96 per cent hemoglobin (14.5 Gm per hundred cubic centimeters), 4,800,000 erythrocytes, 72 per cent leukocytes, a color index of 1.40 per cent polymorphonuclear leukocytes (segmented forms 39, stab forms 1), 44 per cent small lymphocytes, 5 per cent eosinophils and 2 per cent monocytes. The erythrocyte and differential white cell counts were within normal limits.

The patient has a brother aged 4½ years, who is living and well. One sister died five years ago as a result of lead poisoning. Both parents are living and well.

#### DISCUSSION

DR H. H. PERLMAN: I thought there might be a frustration problem behind the behavior in this case and questioned the father and mother independently, without result. I am tempted to use an impervious dressing over the scalp.

DR THOMAS BUTTERWORTH, Reading, Pa.: I suggest giving the child a close haircut, down to actual baldness. I have found that eventually such children cease pulling their hair out.

#### Calcified Sebaceous Cysts, Lupus Erythematosus of the Face Presented by DR E. R. GROSS

G. S., a white woman aged 60, undernourished and seeming older than her calendar age, presents discrete, erythematous, scaly lesions on each cheek. Multiple nodular, yellowish and firm lesions are present on the fingers and at the base of the palms, these secrete a sebaceous material. The disease had its onset in 1935 as "bumps on the fingers" and became progressively worse with the development of new lesions. Two years ago an eruption developed on the face.

Physical examination revealed no gross abnormalities.

A complete blood count was essentially normal. The calcium and cholesterol contents of the blood were 11.5 and 210 mg, respectively, per hundred cubic centimeters. The urine was normal.

The patient has been treated with sodium bismuth triglycollamate ("bismurate tablets") for the lupus erythematosus since Oct. 5, 1945, with pronounced improvement, and parathyroid injection U. S. P., 100 units, twice a month for six months.

#### DISCUSSION

DR V. PARDO-CASTELLO, Habana, Cuba (by invitation): I agree with the diagnosis of lupus erythematosus of the face and the diagnosis of calcium deposits, but the diagnosis of sebaceous cysts with the calcium deposits would have to be proved. For lesions in some places on the palms, I do not think the diagnosis would stand. Biopsy is indicated.

DR D. M. PILLSBURY: It is my impression that atherosclerosis is present.

DR E R GROSS When I first saw this patient, about eight months ago, I thought she had scleroderma. All the involved regions were calcified and stony hard. After four months of treatment with parathyroid injections the lesions softened, and I was able to express sebaceous material from many of them. A roentgenogram of the hands revealed no involvement of the long bones. A few weeks ago I prescribed the use of soluble bismuth (bistrimate), and the lesions on the face have improved about 70 per cent. This diagnosis is a tentative one. I should like therapeutic suggestions.

DR HERMAN BEERMAN There is a form of scleroderma associated with calcinosis, the so-called Thibierge-Weissenbach syndrome.

DR PATRICIA DRANT I think a chemical analysis of the expressed material should be made.

DR FRED D WLIDMAN Many of us recall a case of steatocystoma multiplex presented before this society in which there was a mixture of gritty material. Considerable discussion arose as to the composition of this material. If Dr Gross were willing to substitute the word "greasy" for "sebaceous," it would answer some of the objections that have been raised. These lesions are deep and can extend into the subcutaneous fat which is abundant on the palms, and it might be that it was this fat that was expressed. One can easily examine the gritty material to settle the question whether it is calcium or something else by adding a 10 per cent solution of sulfuric acid and placing a cover slip over it. If the cover slip bubbles up, the presence of calcium carbonate is indicated.

DR MORRIS MARKOWITZ A determination of the calcium and phosphate content is important. Even if the serum calcium is abnormal, the presence of calcinosis is not proved. I do not know whether the ratio between the calcium and the phosphorus has been determined in this case. An increase in the phosphorus level is usually associated with calcinosis cutis.

DR JOHN F WILSON I recently saw a lesion strongly resembling the lesions on the finger of this patient. Microscopic examination revealed xanthomatous giant cell development in the tendon sheath. Though tumors may appear in a case of long standing, other changes secondary to the original tumor may develop.

DR FRED D WEIDMAN Many years ago Pollitzer presented a case of calcareous change in a xanthomatous lesion.

DR THOMAS BUTTERWORTH, Reading, Pa. Was the test for cholesterol made after the patient had been on a low fat diet for two weeks?

#### A Case of Bowen's Disease Presented by DR M H SAMITZ

E S, a white man aged 78, presents a single patch 7.5 by 5 cm on the anterior aspect of the left foot. The border is slightly elevated. The skin is thinned over a red-brown base, which shows through in several small, erosive areas as granulation-like tissue. The eruption is of ten years' duration.

General physical examination revealed no gross abnormalities.

The histologic report on the biopsy, by Dr Fred D Weidman, was as follows: "In the section which represented one-half the specimen nothing diagnostic appeared. In the other half, however, there were parts of this highly acanthotic and hyperkeratotic epidermis which exhibited the features of Bowen's disease. Thus, so far as judgment would permit (only a part of the entire thickness of the epidermis was included for study), the basement membrane was intact, but the epidermal cells were neoplastic. Their nuclei in general were large and hyperchromatic, in addition, there were numerous cells which could be classified as Bowen's cells. In keeping, too, with Bowen's disease was the fact that there was an abundant lymphocytic infiltration of the corium."

Paste of resorcinol was prescribed as a palliative until the lesion could be treated by electrocoagulation.

## DISCUSSION

DR THOMAS BUTTERWORTH, Reading, Pa Without a biopsy, I should consider the eruption lichen planus

DR MEYER L NIEDELMAN I suggest roentgenotherapy rather than electrocoagulation, since healing will be slow at the patient's age

DR BERTRAM SHAFFER What effect would solid carbon dioxide have?

DR CARROLL S WRIGHT It is the ideal means of treatment, but it would make the patient uncomfortable for some time I should not want to do that to a patient 78 years of age

**Disseminated Lupus Erythematosus Treated with Sodium Bismuth Triglycollamate ("Bistrimate Tablets")** Presented by DR CARROLL S WRIGHT and DR E R GROSS

F K, a white woman aged 38, was first seen on March 5, 1945, with disseminated lupus erythematosus involving the chest, forearms and lips, which had been present for six months However, the onset dated back to August 1941, at which time the eruption followed a sunburn Since then she has had remissions and exacerbations but has never been entirely free of the lesions

At the onset she was hospitalized, had complete laboratory studies, which revealed nothing significant, and received one injection of a bismuth compound, which apparently aggravated the existing eruption She is presented to show the pronounced improvement of the lupus erythematosus with sodium bismuth triglycollamate therapy, which was started on March 5, 1945, with 2 tablets (410 mg each) three times a day, after meals This is the first time that she has been relatively free from her lupus erythematosus She is feeling much better generally No reactions were encountered with this therapy Thiamine chloride, 10 mg, has been given subcutaneously as a placebo at two week intervals, to keep the patient under observation

## DISCUSSION

DR HERMAN BEERMAN Have you control cases treated with sobisminol mass?

DR CARROLL S WRIGHT We have treated about 40 patients with syphilis, about 77 with lupus erythematosus and a few with other dermatoses with this preparation The response in patients with lupus erythematosus has been remarkable throughout, though a few could not tolerate it and we had to discontinue its use

DR E R GROSS Sodium bismuth triglycollamate has a complex formula and was intended primarily for syphilitic therapy Patients have now received this therapy for four or five months It has been characterized by the absence of reactions except for bismuth stomatitis We have seen no signs of renal irritation, there has been a daily excretion of 2 to 4 mg of bismuth in the urine We have not seen any fixed eruption However, gastrointestinal disturbances with anorexia, and perhaps nausea and vomiting, have occasionally appeared at the beginning, but if the patient continues to take the drug, this complication is soon overcome, perhaps by cutting down the dose or sometimes by discontinuing the use of the drug temporarily We believe that the good results are due to its being soluble orally and in large measure readily absorbable Sodium bismuth triglycollamate differs from sobisminol mass

DR THOMAS BUTTERWORTH, Reading, Pa The fact that this drug is effective by mouth while other bismuth preparations are ineffective by intramuscular injection suggests that the intestine is the source of the photosensitizing agent in lupus erythematosus The disease is of unknown origin, but administration of the bismuth directly into the intestinal tract may accomplish more than injection

DR CARROLL S WRIGHT I think that Dr Butterworth's suggestion is a good one and that the results with this drug may give a clue to the cause of lupus erythematosus

**Keratotic Lupus Erythematosus Treated with Sodium Bismuth Triglycollamate ("Bistrimate Tablets")** Presented by DR CARROLL S WRIGHT and DR E R GROSS

M C, a white woman aged 24, had a keratotic lesion of lupus erythematosus over the bridge of the nose and a discoid patch of lupus erythematosus on the left cheek, of two years' duration. These lesions were said to have followed a burn with bacon grease. Treatment with sodium bismuth triglycollamate was started on Sept 25, 1945, with 2 tablets (410 mg each) three times daily, after meals. She also received 0.25 cc of liver extract subcutaneously at weekly intervals. She is presented to show the decided improvement following oral therapy with sodium bismuth triglycollamate.

DISCUSSION

DR CARROLL S WRIGHT In all fairness, I must say that this patient was permitted to rub petrolatum into the crusted area, which probably removed part of the crust. She came in with a heavy scale, which quickly came off, and that alone would have produced decided improvement in her appearance. However, the lesions are undergoing involution.

**Disseminated Lupus Erythematosus Treated with Sodium Bismuth Triglycollamate** Presented by DR CARROLL S WRIGHT and DR E R GROSS

E B, a white woman aged 26, was first seen with disseminated lupus erythematosus of the face, chest, back and forearms, which had its onset in March 1945. On August 22 she was given a bismuth preparation parenterally, without apparent improvement. On September 10 treatment was started with sodium bismuth triglycollamate, 2 tablets three times daily, after meals. The eruption has shown decided improvement since this therapy was instituted. Liver extract, 0.25 cc, was given subcutaneously as a placebo while the patient was being treated with sodium bismuth triglycollamate.

DISCUSSION

DR E R GROSS Before this patient came to see us, she had been confined to bed with increase in temperature and painful joints. At the time she came to the office she still had a slight elevation of temperature. We felt that she had disseminated lupus erythematosus and started treatment with injections of a bismuth compound, without apparent improvement. She was then given sodium bismuth triglycollamate, and the lesions underwent involution after a week's treatment. The back and lips were involved, but are now entirely clear.

DR DONALD M PILLSBURY This woman presents a characteristic picture of acute disseminated lupus erythematosus. She appears ill. I doubt whether she will live a year.

DR CARROLL S WRIGHT That is the type of case, I admit, in which there is not much hope. I agree with you that she may die within a year.

NOTE (Dr Carroll S Wright)—One month after the presentation of this patient she had a severe recurrence. She then left the city, and nothing further has been heard from her.

## Book Reviews

**Allergy in Practice** By Samuel M. Feinberg, M.D., with the collaboration of Oren C. Durham and Carl A. Dragstedt, Ph.D., M.D. Second revised edition. Price, \$10.50. Pp. 838, with 35 illustrations. Chicago: The Year Book Publishers, Inc., 1946.

This book is a presentation of the subject of allergy with an attempt to cover the field and to emphasize its practical aspects. The first edition was published in 1944, but the author feels that a second edition is justified because of the recent progress in experimental and clinical fields of allergy.

There are thirty chapters beginning with an introduction and a history, anaphylaxis, hypersensitiveness in man, general causes of allergic disease and epidermal allergens. There follows a complete chapter by Oren C. Durham, Chief Botanist of Abbott Laboratories, on pollens and pollen allergy covering one hundred and four pages with photographs of the important plants producing pollen allergy and charts of their geographic distribution. The chapter on allergy to fungi is unusually thorough, largely because of the author's interest and work in this field. In the following chapters, miscellaneous inhalants, food allergy, allergy to drugs, allergy to injected substances, internal allergens and allergy to physical agents are treated. Chapters on asthma, hay fever and the treatment of allergic diseases and a chapter on hyperesthetic rhinitis cover two hundred and thirty-nine pages. The subjects which should be of most interest to the dermatologist are found in the next three chapters comprising sixty-nine pages. These are urticaria and angioneurotic edema, atopic dermatitis and dermatophytosis and contact eczema. There follow chapters on allergy of the digestive tract, migraine and allergic headaches, allergy of the eye and miscellaneous manifestations and an important chapter on preparation of allergens. The next chapter is on histamine in anaphylaxis and allergy by Carl A. Dragstedt, Professor and Chairman of the Department of Pharmacology, Northwestern University Medical School. In the final chapter on histamine antagonists, the newer drugs "benadryl hydrochloride" N N R (diphenhydramine hydrochloride) and "pyribenzamine hydrochloride" N N R (tripelennamine hydrochloride) are discussed.

Until one arrives at the chapter on atopic eczema and dermatophytosis one is impressed by the author's sincere attempt to present the subject of allergy in a clear manner and by his conservative handling of controversial subjects. Obviously, there are statements or implications with which some may be expected to disagree. For instance, it is doubtful whether the majority of dermatologists will agree with this statement, on page 659: "In spite of the present unsatisfactory status of skin tests in urticaria, I believe that in difficult and recurring cases they are justified because of the possibility that positive reactions when they do occur, may be the means of arriving at a practical and rapid solution of the problem." The author had previously correctly stated that in his experience cutaneous tests are of value in only a small percentage of cases of urticaria. Also, the following statement regarding the beneficial effects of the injection of fungous extracts for the treatment of dermatophytosis is contrary to the belief of those who have had wide experience in this field: "I believe that desensitizing doses, given with caution, can accomplish some good. I have the impression that patients who show an immediate reaction are particularly likely to be benefited."

The chapter on atopic dermatitis and dermatophytosis comprises twenty-one pages. One wonders why these two subjects should be included in the same chapter. Many will disagree with the opening sentence of this chapter: "Atopic dermatitis is a skin inflammation of an allergic nature and of internal origin."

The following statements will likewise not be generally accepted by those having experience with patients with atopic dermatitis "Generally, these fluctuations in intensity are due to changes or modifications of the allergic substances to which the person is exposed" "Food allergy in atopic dermatitis is common" "After the history is obtained, it is usually necessary to perform diagnostic skin tests The procedure of choice is the scratch test" "Contrary to opinions held in some quarters, I am definitely of the opinion that desensitization treatment in atopic dermatitis should be considered as seriously as it is in allergic respiratory tract manifestations" It is the opinion of the reviewer that the author, when his theories regarding this subject are so contrary to the theories of almost all dermatologists with experience, should have presented not only his own views but also the views of the majority of workers in this field Thousands of patients of all ages, from infancy through adulthood, with atopic dermatitis have been tested with as many as several hundred scratch tests each, many show no reaction whatever In patients who do show positive reactions the elimination or avoidance of the suspected agent and the attempts toward desensitization have seldom resulted in any alleviation of atopic dermatitis Why, in the light of the experiences of others and of our present knowledge, should the indiscriminate testing of these patients be further encouraged?

While the value of carefully determining the history in all phases of allergic conditions is repeatedly emphasized, even further emphasis of this extremely important procedure in the investigation of allergic conditions would be of value particularly as it relates to contact dermatitis

While there is considerable disagreement regarding the relationship between allergy and emotional disturbances, most observers will agree with the author's statement, "A personality change in an allergic person is the result and not the cause of allergic symptoms It is not denied that emotional, psychic or nervous factors modify or incite the allergic attack" One wonders whether it would not have been worth while to have devoted more space to the recognition and attempted management of this phase of the allergic problem as a therapeutic procedure

A short resume following most chapters is a valuable asset There is an extensive bibliography at the end of each chapter and an index which is most useful

**Penicillin Therapy and Control in the Twenty-First Army Group** Published under the direction of the Director of Medical Services, Twenty-First Army Group Pp 365 Printing and Stationery Service, British Army of the Rhine, 1945

This book is a compilation of sixty reports and articles by members of the Royal Army Medical Corps, Twenty-First Army Group It includes many subjects other than penicillin therapy, such as those dealing with the surgical treatment of war wounds In the introduction by the consulting surgeon it is modestly titled a "brochure" but it is definitely more than "a pamphlet dealing with a subject of passing interest" because this publication is the useful result of a great amount of practical investigation carried out in the difficult circumstances arising in an active campaign

In the section devoted to the use of penicillin in the treatment of diseases of the skin, two methods of local application are described (1) as a solution containing 200 to 500 units per cubic centimeter of sterile water and (2) as an emulsion of 30 per cent Lanette wax in water containing 200 to 500 units per gram The solution was sprayed on the skin three times daily in the clinic, and the emulsion, when used, was applied by the patient, with equally good results in the treatment of impetigo, sycosis barbae, ecthyma and infected dermatitis of various types In all these diseases except impetigo it was necessary to supplement penicillin with other drugs to complete the cure after penicillin had dealt with the "infective element" of the disease The drug was found to be useful in the treatment of furuncles and carbuncles when administered parenterally

The book should be most useful to physicians interested in the broad field of penicillin therapy in general medical and surgical diseases

**The Girls They Left Behind** By Brethe Hartmann, M D Price, 12 kroner  
Pp 208 Copenhagen Ejnar Munksgaard Forlag, 1946

This monograph presents the results of a study of the effects of the war and the German occupation on the incidence of prostitution and venereal disease in Denmark. It is based on data gathered principally in the police courts. A large number of case histories is included in which the family background, religion, education, occupation, personal interests, sex history and medical facts of individual girls are detailed.

In 1936, Tage Kemp wrote as follows "We have made such progress in the campaign against syphilis in Denmark, and especially in Copenhagen, that we may regard the disease as an exotic malady, like cholera and smallpox, usually brought into the country by seafarers and travelers from foreign lands." Unfortunately, this roseate situation did not last long. After the German occupation in April 1940 the prevalence of syphilis increased rapidly, so that in 1944 it was 83 times that in 1938.

In 1939, the women examined in the police courts were almost exclusively professional prostitutes, and 15 per cent were infected with venereal diseases. However, in 1943, as a result of war, overcrowding, family dislocations, German occupation and other factors, the girls examined belonged to younger age groups and were chiefly of nonprofessional status, and the incidence of venereal diseases among them was 55 per cent.

The book is well written in English, but it will have greater interest for the sociologist and the epidemiologist than for the dermatologist.

**Tropical Medicine** By Sir Leonard Rogers and Sir John W D Megaw Fifth edition Price, \$6.50 Pp 518, with 89 illustrations Baltimore William Wood & Company, 1944

Because of the continued emphasis on a book of a short practical type of text, especially for the general practitioner, there is not a great deal of material on tropical dermatology included. The emphasis has been on tropical medicine, especially in India. The section on microscopy is of practical value. The following dermatologic diseases are considered briefly: chagomata, leishmaniasis, mycoses, tropical ulcer, ainhum, tungiasis, Hodgkin's disease, leprosy, yaws, plague, carbuncle, pellagra, ariboflavinosis, dermatitis solaris, larva migrans and syphilis.

Because of brevity, some controversial material in regard to tropical dermatology is included. This is especially true of "espundia," in which oronasal involvement is reported to occur in some 80 per cent of the cases. This figure is unusually high except in some heavy endemic areas. Contrary to the authors, oronasal involvement as yet has not been reported in Mexico. This is another argument for discarding a confusing colloquial term in general literature such as "espundia" and substituting a clearer term such as "American cutaneous leishmaniasis with mucosal involvement, primary (or metastatic)." In regard to the search for microfilariae in onchocerciasis in America, these parasites are found easily. Follicular keratoses are not noted in the description of vitamin A deficiency. The remarks on syphilis in India are interesting in that there is a discussion of the rare complications of primary syphilitic pulmonary atheroma. Also, although it is indicated, as usual, that tabes and paresis are rare in the tropics (diagnosis?) paraplegia due to syphilis is reported as a "very common late manifestation in India." The remarks on the incidence of tumors in India as compared to London are also interesting, "malignant epithelial tumors" showed excess in India of epithelioma of the skin in relation with the frequency of chronic ulcerative processes. Also, epithelioma of the penis is more common in uncircumcised Hindus than in the circumcised Mohammedans. Epithelioma of the inside of the cheek often follows chewing betel nut with lime.

It is chiefly, then, the general practitioner in India who will find this small volume of definite practical value.

**The Problem of Lupus Vulgaris** By Robert S Aitken, M D, Lecturer in Diseases of the Skin, Edinburgh University First edition Price, \$4 Pp 76, with 31 illustrations in color and black and white Baltimore Williams & Wilkins Company, 1946

This small manual, written by a man with many years of experience in treating lupus vulgaris, is a good resume of the author's personal experience with this disease. However, it is unfortunate that an advance in the treatment of lupus vulgaris as important as the use of vitamin D<sub>2</sub>, reported by Charpy in 1943, was not known to the author. This new development in therapy is not referred to at all.

As a survey of what the problem of lupus vulgaris is, both to the individual and to the community, and as an evaluation of technic of treatment with special reference to the fine results obtained by the Finsen-Lomholt lamp, this book would be valuable to physicians, including general practitioners, who encounter lupus vulgaris.

The book is divided into five chapters. These chapters cover the clinical features of the disease, treatments in general, ultraviolet irradiation, tuberculin treatment and the social and economic problems of lupus vulgaris.

In the chapter on the clinical features of the disease, the characteristics of lupus vulgaris of various types are described. The author also discusses the relationship between lupus vulgaris and tuberculosis elsewhere in the body and states that lupus is rarely accompanied or followed by pulmonary tuberculosis. The geographic distribution and the age and sex incidence of lupus vulgaris are discussed, as well as the etiology, differential diagnosis and prognosis. It is said to be twice as common in women as in men. The onset is usually in childhood or adolescence, and the bovine and human tubercle bacillus in attenuated form is the responsible organism, with the focus of infection nearly always internal.

The main part of the book covers the treatment of lupus vulgaris. This is divided into three chapters, on treatment in general, on treatment with ultraviolet irradiation and on treatment with tuberculin. The Gerson salt-free diet is said to be impractical, and the use of roentgen ray is condemned. Lomholt is quoted as saying that he never saw a case of carcinoma on lupus unless there had been previous roentgen ray treatment.

The history of the development of the Finsen-Lomholt carbon arc lamp, a description of its mechanism and its faults and the general technic of its use, as well as comparison of this lamp with mercury vapor lamps, are given in the chapter on ultraviolet irradiation. Here the results of local ultraviolet therapy combined with general ultraviolet irradiation are evaluated.

The third chapter on treatment deals with the use of tuberculin in the treatment of lupus vulgaris, and excellent results are reported with either tuberculin ointment or subcutaneous injections in carefully regulated doses. Treatment with tuberculin is recommended when ultraviolet irradiation cannot be obtained.

The final chapter in the book deals with the economic and social aspects of lupus vulgaris.

**Practical Handbook of the Pathology of the Skin** By J M H MacLeod and Isaac Muende Third edition Price, \$9 Pp 416, with 27 colored and 125 black and white illustrations New York Paul B Hoeber, Inc, 1946

Strictly speaking, this is not a new edition. It is a reprint. The number of pages in the book is exactly the same, and the various topics appear on the same pages in the second as in the third edition. This edition is printed on heavy enamel stock, and accordingly the book is considerably thicker than the preceding one.

As its title indicates, the subject of pathology is discussed in all of its aspects: histologic technic, embryology, anatomy, congenital anomalies, tissue changes in disease, animal parasites, bacteriology and mycology.

The illustrations are the features that are the most needed in dermatology, and it is regrettable that the text concerning the histopathology is not more ample, but the extended scope of the book has doubtless prevented this. The book continues to be the most useful one of its kind in dermatology.

**Penicillin in Neurology** By Arthur Earl Walker, M D, and Herbert C Johnson, M D First edition Price, \$5 Pp 216, with 95 illustrations Springfield, Ill Charles C Thomas, Publisher, 1946

The authors have reviewed the literature relative to the effects of antibiotics on the central nervous system and have presented their own interesting experimental and clinical data Major attention is given to the toxic effects of penicillin when administered parenterally, when applied directly to nervous tissue or when injected into the lateral ventricles, the cisterna cerebellomedullaris or other subarachnoid space The therapeutic value of penicillin and other antibiotics in various infectious and noninfectious diseases of the central nervous system has been covered adequately

Of chief interest to the dermatologist is the section devoted to the treatment of syphilis of the central nervous system The subject is considered briefly, and it is noteworthy that not one of the twenty references in the bibliography pertain to articles published later than 1945 The tempo of investigation in neurosyphilis has been so rapid that it has outstripped the material published in this book Reference is made to the danger of serious reactions resembling Heineheimer's reaction in the central nervous system, when therapeutic doses of penicillin are initiated and to the method of obviating such reactions

The book is well written and profusely illustrated, but it has greater value for the neurologist and the neurosurgeon than for the dermatologist

**Allergy** By Erich Urbach, M D, and Philip M Gottlieb, M D Second edition Price, \$12 Pp 968, with 412 illustrations New York Grune & Stratton, Inc, 1946

The publication of this second edition only three years after publication of the first indicates a demand by the members of the medical profession for this book The authors have added 21 new illustrations and 1,300 new references after omitting a few hundred older ones New sections are added on psychosomatic aspects, the Rh factor, allergic bronchitis, allergic cough and eosinophilic erythredema The index of authors comprises 26 pages and the index of subjects 33 pages

The book is divided into three parts The first deals with the fundamentals of allergy, the second, with etiologic agents of allergic diseases and the third part with symptoms and therapy of allergic diseases The allergic diseases of the different organs and systems of the body are taken up Almost 100 pages are devoted to cutaneous diseases

The reviewer has paid special attention to the part relating particularly to dermatology He is convinced that the dermatologist will find this book stimulating because of an enormous amount of interesting and important topics This book may be used as a reference book by the general medical practitioner, but the dermatologist will profit considerably by reading this textbook from beginning to end

Some of the personal opinions of the authors, for instance as to the value of propeptans, may be in disagreement with the opinions of most of the observers in this country Nevertheless, it does not detract from the value of the book as the authors cite references for opinions different from their own



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